10/801 671

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     (FILE 'HOME' ENTERED AT 11:22:18 ON 01 APR 2005)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 11:22:41 ON 01 APR 2005
L1       1301511 S KINASE?
L2          1597 S SERINE (W) ARGININE
L3           326 S L1 AND L2
L4       7000132 S CLON? OR EXPRESS? OR RECOMBINANT
L5           207 S L3 AND L4
L6           116 S HUMAN AND L5
L7           696 S "SERINE ARGININE RICH"
L8            78 S L6 AND L7
                 E BOYDS J Y/AU
                 E YE J/AU
L9          1892 S E3
                 E YAN C/AU
L10         1117 S E3
                 E KETCHUM K A/AU
L11          480 S E3-E8
                 E DIFRANCESCO V/AU
L12          117 S E3-E4
                 E BEASLEY E M/AU
L13        31699 S E3\
L14          324 S E3
L15         3624 S L9 OR L10 OR L11 OR L12 OR L14
L16            1 S L2 AND L15
L17            1 S L7 AND L15
L18            1 S L6 AND L15
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                   (ROSPATENT) added to list of core patent offices covered
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                   data from INPADOC
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FILE 'LIFESCI' ENTERED AT 11:22:41 ON 01 APR 2005


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=> s kinase?
L1     1301511 KINASE?

=> s serine (w) arginine
L2        1597 SERINE (W) ARGININE

=> s l1 and l2
L3         326 L1 AND L2

=> s clon? or express? or recombinant
   4 FILES SEARCHED...
L4     7000132 CLON? OR EXPRESS? OR RECOMBINANT

=> s l3 and l4
L5         207 L3 AND L4

=> s human and l5
L6         116 HUMAN AND L5

=> dup rem l6
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=> s "serine arginine rich"
L7         696 "SERINE ARGININE RICH"

=> s l6 and l7
L8          78 L6 AND L7

=> dup rem l8
COMMAND INTERRUPTED
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=> d 1-78 ibib ab
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L8 ANSWER 1 OF 78 MEDLINE on STN
ACCESSION NUMBER: 2004270625 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15010457
TITLE: Manipulation of alternative splicing by a newly developed inhibitor of Clks.
AUTHOR: Muraki Michiko; Ohkawara Bisei; Hosoya Takamitsu; Onogi Hiroshi; Koizumi Jun; Koizumi Tomonobu; Sumi Kengo; Yomoda Jun-ichiro; Murray Michael V; Kimura Hiroshi; Furuichi Kiyoshi; Shibuya Hiroshi; Krainer Adrian R; Suzuki Masaaki; Hagiwara Masatoshi
CORPORATE SOURCE: Laboratory of Gene Expression, School of Biomedical Science, Department of Functional Genomics, Medical Research Institute, Tokyo Medical & Dental University, Japan.
SOURCE: Journal of biological chemistry, (2004 Jun 4) 279 (23) 24246-54. Electronic Publication: 2004-03-08. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 20040602
Last Updated on STN: 20040709
Entered Medline: 20040708

AB The regulation of splice site usage provides a versatile mechanism for controlling gene **expression** and for the generation of proteome diversity, playing an essential role in many biological processes. The importance of alternative splicing is further illustrated by the increasing number of **human** diseases that have been attributed to mis-splicing events. Appropriate spatial and temporal generation of splicing variants demands that alternative splicing be subjected to extensive regulation, similar to transcriptional control. The Clk (Cdc2-like **kinase**) family has been implicated in splicing control and consists of at least four members. Through extensive screening of a chemical library, we found that a benzothiazole compound, TG003, had a potent inhibitory effect on the activity of Clk1/Sty. TG003 inhibited SF2/ASF-dependent splicing of beta-globin pre-mRNA in vitro by suppression of Clk-mediated phosphorylation. This drug also suppressed **serine/arginine-rich** protein phosphorylation, dissociation of nuclear speckles, and Clk1/Sty-dependent alternative splicing in mammalian cells. Consistently, administration of TG003 rescued the embryonic defects induced by excessive Clk activity in Xenopus. Thus, TG003, a novel inhibitor of Clk family will be a valuable tool to dissect the regulatory mechanisms involving **serine/arginine-rich** protein phosphorylation signaling pathways in vivo, and may be applicable for the therapeutic manipulation of abnormal splicing.

L8 ANSWER 2 OF 78 MEDLINE on STN
ACCESSION NUMBER: 2004041731 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14602710
TITLE: Glycogen synthase **kinase**-3 plays a crucial role in tau exon 10 splicing and intranuclear distribution of SC35. Implications for Alzheimer's disease.
AUTHOR: Hernandez Felix; Perez Mar; Lucas Jose J; Mata Ana M; Bhat Ratan; Avila Jesus
CORPORATE SOURCE: Centro de Biologia Molecular Severo Ochoa Consejo Superior de Investigaciones Cientificas/CSIC/Universidad Autonoma, Fac. Ciencias. Universidad Autonoma de Madrid, Cantoblanco, 28049 Madrid, Spain.
SOURCE: Journal of biological chemistry, (2004 Jan 30) 279 (5)

3801-6. Electronic Publication: 2003-11-05.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 20040127
Last Updated on STN: 20040312
Entered Medline: 20040311

AB Tauopathies, including Alzheimer's disease, are neurodegenerative disorders in which tau protein accumulates as a consequence of alterations in its metabolism. At least three different types of alterations have been described; in some cases, an aberrant mRNA splicing of tau exon 10 occurs; in other cases, the disorder is a consequence of missense mutations and, in most cases, aberrant tau hyperphosphorylation takes place. Glycogen synthase **kinase**-3 (GSK-3) has emerged as a key **kinase** that is able to interact with several proteins involved in the etiology of Alzheimer's disease and other tauopathies. Here, we have evaluated whether GSK-3 is also able to modulate tau-mRNA splicing. Our data demonstrate that GSK-3 inhibition in cultured neurons affects tau splicing resulting in an increase in tau mRNA containing exon 10. Pre-mRNA splicing is catalyzed by a multimolecular complex including members of the **serine/arginine-rich** (SR) family of splicing factors. Immunofluorescence studies showed that after GSK-3 inhibition, SC35, a member of the SR family, is redistributed and enriched in nuclear speckles and colocalizes with the **kinase**. Furthermore, immunoprecipitated SC35 is phosphorylated by **recombinant** GSK-3beta. Phosphorylation of a peptide from the SR domain by GSK-3 revealed that the peptide needs to be prephosphorylated, suggesting the involvement of a priming **kinase**. Our results demonstrate that GSK-3 plays a crucial role in tau exon 10 splicing, raising the possibility that GSK3 could contribute to tauopathies via aberrant tau splicing.

L8 ANSWER 3 OF 78 MEDLINE on STN
ACCESSION NUMBER: 2003148292 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12615334
TITLE: An early ancestor in the evolution of splicing: a Trypanosoma cruzi **serine-arginine-rich** protein (TcSR) is functional in cis-splicing.
AUTHOR: Portal Daniel; Espinosa Joaquin M; Lobo Guillermo S; Kadener Sebastian; Pereira Claudio A; De La Mata Manuel; Tang Zhaohua; Lin Ren-Jang; Kornblihtt Alberto R; Baralle Francisco E; Flawia Mirtha M; Torres Hector N
CORPORATE SOURCE: Facultad de Ciencias Exactas y Naturales, Instituto de Investigaciones en Ingenieria Genetica y Biologia Molecular, Consejo Nacional de Investigaciones Cientificas y Tecnicas, Universidad de Buenos Aires, Buenos Aires, Argentina.
SOURCE: Molecular and biochemical parasitology, (2003 Mar) 127 (1) 37-46.
Journal code: 8006324. ISSN: 0166-6851.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 20030401
Last Updated on STN: 20030713
Entered Medline: 20030711

AB A novel **serine-arginine-rich** protein designated TcSR was identified in Trypanosoma cruzi. The deduced amino

acid sequence reveals that TcSR is a member of the SR protein family of splicing factors that contains two RNA-binding domains at the N-terminal side and several **serine-arginine** repeats at the COOH-terminus. Over **expression** of either TcSR or the **human** SR-protein associated splicing factor/splicing factor 2 (ASF/SF2) in wild-type Schizosaccharomyces pombe, provoked an elongated phenotype similar to that of fission yeast over **expressing** the SR-containing splicing factor Prp2, a U2AF(65) orthologue. When a double mutant strain lacking two SR protein-specific protein **kinases** was used, **expression** of TcSR or **human** SR ASF/SF2 splicing factor reverted the mutant to a wild-type phenotype. Transient **expression** of TcSR in HeLa cells stimulated the inclusion of the EDI exon of **human** fibronectin in an in vivo functional alternative cis-splicing assay. Inclusion was dependent on a splicing enhancer sequence present in the EDI exon. In addition, TcSR and peptides carrying TcSR-RS domain sequences were phosphorylated by a **human** SR protein **kinase**. These results indicate that TcSR is a member of the SR splicing network and that some components common to the trans- and cis-splicing machineries evolved from the early origins of the eukaryotic lineage.

L8 ANSWER 4 OF 78 MEDLINE on STN
ACCESSION NUMBER: 2003056108 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12565823
TITLE: The kic1 **kinase** of schizosaccharomyces pombe is a CLK/STY orthologue that regulates cell-cell separation.
AUTHOR: Tang Zhaohua; Mandel Linda L; Yean Shyue-Lee; Lin Cindy X; Chen Tina; Yanagida Mitsuhiro; Lin Ren-Jang
CORPORATE SOURCE: Division of Molecular Biology, Beckman Research Institute of the City of Hope, Duarte, CA 91010, USA.
CONTRACT NUMBER: 1 S10 RR01462-01 (NCRR)
SOURCE: Experimental cell research, (2003 Feb 1) 283 (1) 101-15. Journal code: 0373226. ISSN: 0014-4827.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20030205
Last Updated on STN: 20030313
Entered Medline: 20030312

AB The CLK/STY **kinases** are a family of dual-specificity protein **kinases** implicated in the regulation of cellular growth and differentiation. Some of the **kinases** in the family are shown to phosphorylate **serine-arginine-rich** splicing factors and to regulate pre-mRNA splicing. However, the actual cellular mechanism that regulates cell growth, differentiation, and development by CLK/STY remains unclear. Here we show that a functionally conserved CLK/STY **kinase** exists in Schizosaccharomyces pombe, and this orthologue, called Kic1, regulates the cell surface and septum formation as well as a late step in cytokinesis. The Kic1 protein is modified in vivo, likely by phosphorylation, suggesting that it can be involved in a control cascade. In addition, kic1(+) together with dsk1(+), which encodes a related SR-specific protein **kinase**, constitutes a critical in vivo function for cell growth. The results provide the first in vivo evidence for the functional conservation of the CLK/STY family through evolution from fission yeast to mammals. Furthermore, since cell division and cell-cell interaction are fundamental for the differentiation and development of an organism, the novel cellular role of kic1(+) revealed from this study offers a clue to the understanding of its counterparts in higher eukaryotes.

L8 ANSWER 5 OF 78 MEDLINE on STN
ACCESSION NUMBER: 2003055504 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12565863
TITLE: Effect of cisplatin treatment on speckled distribution of a **serine/arginine-rich** nuclear protein CROP/Luc7A.
AUTHOR: Umehara Hiroshi; Nishii Yoichi; Morishima Masaki; Kakehi Yoshiyuki; Kioka Noriyuki; Amachi Teruo; Koizumi Jun; Hagiwara Masatoshi; Ueda Kazumitsu
CORPORATE SOURCE: Laboratory of Cellular Biochemistry, Division of Applied Life Sciences, Kyoto University Graduate School of Agriculture, Kyoto 606-8502, Japan.
SOURCE: Biochemical and biophysical research communications, (2003 Feb 7) 301 (2) 324-9.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 20030205
Last Updated on STN: 20030417
Entered Medline: 20030415

AB The C-half of cisplatin resistance-associated overexpressed protein (CROP), an SR-related protein, comprises domains rich in arginine and glutamate residues (RE domain), and is rich in arginine and serine residues (RS domain). We analyzed the role of the individual domains of CROP in cellular localization, subnuclear localization, and protein-protein interaction. CROP fused with green fluorescent protein, GFP-CROP, localized exclusively to the nucleus and showed a speckled intranuclear distribution. The yeast two-hybrid system revealed that CROP interacted with SF2/ASF, an SR protein involved in RNA splicing, as well as CROP itself. The RE and RS domains were necessary for both the intranuclear speckled distribution and the protein-protein interaction. CROP was phosphorylated by mSRPK1, mSRPK2, and Clk1 in vitro, and when cells were treated with cisplatin the subnuclear distribution of GFP-CROP was changed. These results suggest that cisplatin affects RNA splicing by changing the subnuclear distribution of SR proteins including CROP.

L8 ANSWER 6 OF 78 MEDLINE on STN
ACCESSION NUMBER: 2003019245 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12525645
TITLE: Exonic splicing enhancer-dependent selection of the bovine papillomavirus type 1 nucleotide 3225 3' splice site can be rescued in a cell lacking splicing factor ASF/SF2 through activation of the phosphatidylinositol 3-**kinase** /Akt pathway.
AUTHOR: Liu Xuefeng; Mayeda Akila; Tao Mingfang; Zheng Zhi-Ming
CORPORATE SOURCE: HIV and AIDS Malignancy Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.
SOURCE: Journal of virology, (2003 Feb) 77 (3) 2105-15.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 20030115
Last Updated on STN: 20030212
Entered Medline: 20030211

AB Bovine papillomavirus type 1 (BPV-1) late pre-mRNAs are spliced in keratinocytes in a differentiation-specific manner: the late leader 5'

splice site alternatively splices to a proximal 3' splice site (at nucleotide 3225) to **express** L2 or to a distal 3' splice site (at nucleotide 3605) to **express** L1. Two exonic splicing enhancers, each containing two ASF/SF2 (alternative splicing factor/splicing factor 2) binding sites, are located between the two 3' splice sites and have been identified as regulating alternative 3' splice site usage. The present report demonstrates for the first time that ASF/SF2 is required under physiological conditions for the **expression** of BPV-1 late RNAs and for selection of the proximal 3' splice site for BPV-1 RNA splicing in DT40-ASF cells, a genetically engineered chicken B-cell line that **expresses** only **human** ASF/SF2 controlled by a tetracycline-repressible promoter. Depletion of ASF/SF2 from the cells by tetracycline greatly decreased viral RNA **expression** and RNA splicing at the proximal 3' splice site while increasing use of the distal 3' splice site in the remaining viral RNAs. Activation of cells lacking ASF/SF2 through anti-immunoglobulin M-B-cell receptor cross-linking rescued viral RNA **expression** and splicing at the proximal 3' splice site and enhanced Akt phosphorylation and **expression** of the phosphorylated **serine/arginine-rich** (SR) proteins SRp30s (especially SC35) and SRp40. Treatment with wortmannin, a specific phosphatidylinositol 3-**kinase**/Akt **kinase** inhibitor, completely blocked the activation-induced activities. ASF/SF2 thus plays an important role in viral RNA **expression** and splicing at the proximal 3' splice site, but activation-rescued viral RNA **expression** and splicing in ASF/SF2-depleted cells is mediated through the phosphatidylinositol 3-**kinase**/Akt pathway and is associated with the enhanced **expression** of other SR proteins.

L8 ANSWER 7 OF 78 MEDLINE on STN
ACCESSION NUMBER: 2002705381 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12466556
TITLE: PSKH1, a novel splice factor compartment-associated serine **kinase**.
AUTHOR: Brede Gaute; Solheim Jorun; Prydz Hans
CORPORATE SOURCE: Biotechnology Centre of Oslo, University of Oslo, Gaustadalleen 21, N-0349 Oslo, Norway.
SOURCE: Nucleic acids research, (2002 Dec 1) 30 (23) 5301-9. Journal code: 0411011. ISSN: 1362-4962.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20021217
Last Updated on STN: 20021227
Entered Medline: 20021223

AB Small nuclear ribonucleoprotein particles (snRNPs) and non-snRNP splicing factors containing a **serine/arginine-rich** domain (SR proteins) concentrate in splicing factor compartments (SFCs) within the nucleus of interphase cells. Nuclear SFCs are considered mainly as storage sites for splicing factors, supplying splicing factors to active genes. The mechanisms controlling the interaction of the various spliceosome constituents, and the dynamic nature of the SFCs, are still poorly understood. We show here that endogenous PSKH1, a previously **cloned kinase**, is located in SFCs. Migration of PSKH1-FLAG into SFCs is enhanced during co-**expression** of T7-tagged ASF/SF2 as well as other members of the SR protein family, but not by two other non-SR nuclear proteins serving as controls. Similar to the SR protein **kinase** family, overexpression of PSKH1 led to reorganization of co-**expressed** T7-SC35 and T7-ASF/SF2 into a more diffuse nuclear pattern. This redistribution was not dependent on PSKH1 **kinase** activity. Different from the SR protein **kinases**, the SFC-associating features of PSKH1 were located within

its catalytic **kinase** domain and within its C-terminus. Although no direct interaction was observed between PSKH1 and any of the SR proteins tested in pull-down or yeast two-hybrid assays, forced **expression** of PSKH1-FLAG was shown to stimulate distal splicing of an E1A minigene in HeLa cells. Moreover, a GST-ASF/SF2 fusion was not phosphorylated by PSKH1, suggesting an indirect mechanism of action on SR proteins. Our data suggest a mutual relationship between PSKH1 and SR proteins, as they are able to target PSKH1 into SFCs, while forced PSKH1 **expression** modulates nuclear dynamics and the function of co-**expressed** splicing factors.

L8 ANSWER 8 OF 78 MEDLINE on STN
ACCESSION NUMBER: 2001547922 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11585720
TITLE: SKY1 is involved in cisplatin-induced cell kill in Saccharomyces cerevisiae, and inactivation of its **human** homologue, SRPK1, induces cisplatin resistance in a **human** ovarian carcinoma cell line.
AUTHOR: Schenk P W; Boersma A W; Brandsma J A; den Dulk H; Burger H; Stoter G; Brouwer J; Nooter K
CORPORATE SOURCE: Department of Medical Oncology, University Hospital Rotterdam-Daniel den Hoed Cancer Center, Josephine Nefkens Institute, 3000 DR Rotterdam, the Netherlands.
SOURCE: Cancer research, (2001 Oct 1) 61 (19) 6982-6. Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20011015
Last Updated on STN: 20020420
Entered Medline: 20011018

AB The therapeutic potential of cisplatin, one of the most active and widely used anticancer drugs, is severely limited by the occurrence of cellular resistance. In this study, using budding yeast Saccharomyces cerevisiae as a model organism to identify novel drug resistance genes, we found that disruption of the yeast gene SKY1 (**serine/arginine-rich** protein-specific **kinase** from budding yeast) by either transposon insertion or one-step gene replacement conferred cellular resistance to cisplatin. Heterologous **expression** of the **human** SKY1 homologue SRPK1 (**serine/arginine-rich** protein-specific **kinase**) in SKY1 deletion mutant yeast cells restored cisplatin sensitivity, suggesting that SRPK1 is a cisplatin sensitivity gene, the inactivation of which could lead to cisplatin resistance. Subsequently, we investigated the role of SRPK1 in cisplatin sensitivity and resistance in **human** ovarian carcinoma A2780 cells using antisense oligodeoxynucleotides. Treatment of A2780 cells with antisense oligodeoxynucleotides directed against the translation initiation site of SRPK1 led to down-regulation of SRPK1 protein and conferred a 4-fold resistance to cisplatin. The **human** SRPK1 gene has not been associated with drug resistance before. Our new findings strongly suggest that SRPK1 is involved in cisplatin-induced cell kill and indicate that SRPK1 might potentially be of importance for studying clinical drug resistance.

L8 ANSWER 9 OF 78 MEDLINE on STN
ACCESSION NUMBER: 2001484828 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11418604
TITLE: **Cloning** of **human** PRP4 reveals interaction with Clk1.
AUTHOR: Kojima T; Zama T; Wada K; Onogi H; Hagiwara M

CORPORATE SOURCE: Department of Functional Genomics, Medical Research Institute, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8510, Japan.
SOURCE: Journal of biological chemistry, (2001 Aug 24) 276 (34) 32247-56. Electronic Publication: 2001-06-19.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AY029347
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010903
Last Updated on STN: 20030105
Entered Medline: 20010920

AB Prp4 is a protein **kinase** of Schizosaccharomyces pombe identified through its role in pre-mRNA splicing, and belongs to a **kinase** family including mammalian **serine/arginine-rich** protein-specific **kinases** and Clks, whose substrates are **serine/arginine-rich** proteins. We **cloned human** PRP4 (hPRP4) full-length cDNA and the antiserum raised against a partial peptide of hPRP4 recognized 170-kDa polypeptide in HeLa S3 cell extracts. Northern blot analysis revealed that hPRP4 mRNA was ubiquitously **expressed** in multiple tissues. The extended NH(2)-terminal region of hPRP4 contains an arginine/serine-rich domain and putative nuclear localization signals. hPRP4 phosphorylated and interacted with SF2/ASF, one of the essential splicing factors. Indirect immunofluorescence analysis revealed that endogenous hPRP4 was distributed in a nuclear speckled pattern and colocalized with SF2/ASF in HeLa S3 cells. Furthermore, hPRP4 interacted directly with Clk1 on its COOH terminus, and the arginine/serine-rich domain of hPRP4 was phosphorylated by Clk1 in vitro. Overexpression of Clk1 caused redistribution of hPRP4, from the speckled to the diffuse pattern in nucleoplasm, whereas inactive mutant of Clk1 caused no change of hPRP4 localization. These findings suggest that the NH(2)-terminal region of hPRP4 may play regulatory roles under an unidentified signal transduction pathway through Clk1.

L8 ANSWER 10 OF 78 MEDLINE on STN
ACCESSION NUMBER: 1999214190 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10196197
TITLE: The subcellular localization of SF2/ASF is regulated by direct interaction with SR protein **kinases** (SRPKs).
AUTHOR: Koizumi J; Okamoto Y; Onogi H; Mayeda A; Krainer A R; Hagiwara M
CORPORATE SOURCE: Department of Functional Genomics, Medical Research Institute, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113, Japan.
CONTRACT NUMBER: CA13106 (NCI)
SOURCE: Journal of biological chemistry, (1999 Apr 16) 274 (16) 11125-31.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990601
Last Updated on STN: 20020420
Entered Medline: 19990517

AB **Serine/arginine-rich** (SR) proteins play an important role in constitutive and alternative pre-mRNA splicing. The

C-terminal arginine-serine domain of these proteins, such as SF2/ASF, mediates protein-protein interactions and is phosphorylated in vivo. Using glutathione S-transferase (GST)-SF2/ASF-affinity chromatography, the SF2/ASF **kinase** activity was co-purified from HeLa cells with a 95-kDa protein, which was recognized by an anti-SR protein **kinase** (SRPK) 1 monoclonal antibody. **Recombinant** SRPK1 and SRPK2 bound to and phosphorylated GST-SF2/ASF in vitro. Phosphopeptide mapping showed that identical sites were phosphorylated in the pull-down **kinase** reaction with HeLa extracts and by **recombinant** SRPKs. Epitope-tagged SF2/ASF transiently **expressed** in COS7 cells co-immunoprecipitated with SRPKs. Deletion analysis mapped the phosphorylation sites to a region containing an (Arg-Ser)8 repeat beginning at residue 204, and far-Western analysis showed that the region is required for binding of SRPKs to SF2/ASF. Further binding studies showed that SRPKs bound unphosphorylated SF2/ASF but did not bind phosphorylated SF2/ASF. **Expression** of an SRPK2 **kinase** -inactive mutant caused accumulation of SF2/ASF in the cytoplasm. These results suggest that the formation of complexes between SF2/ASF and SRPKs, which is influenced by the phosphorylation state of SF2/ASF, may have regulatory roles in the assembly and localization of this splicing factor.

L8 ANSWER 11 OF 78 MEDLINE on STN
ACCESSION NUMBER: 1999069431 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9852100
TITLE: The cellular localization of the murine **serine/arginine-rich** protein **kinase** CLK2 is regulated by serine 141 autophosphorylation.
AUTHOR: Nayler O; Schnorrer F; Stamm S; Ullrich A
CORPORATE SOURCE: Max Planck Institute for, Am Klopferspitz 18A, D-82152 Martinsried, Germany.. nayler@biochem.mpg.de
SOURCE: Journal of biological chemistry, (1998 Dec 18) 273 (51) 34341-8.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990209
Last Updated on STN: 20020420
Entered Medline: 19990126

AB Pre-mRNA splicing is catalyzed by a multitude of proteins including **serine/arginine-rich** (SR) proteins, which are thought to play a crucial role in the formation of spliceosomes and in the regulation of alternative splicing. SR proteins are highly phosphorylated, and their **kinases** are believed to regulate the recruitment of SR proteins from nuclear storage compartments known as speckles. Recently, a family of autophosphorylating **kinases** termed CLK (CDC2/CDC28-like **kinases**) was shown to phosphorylate SR proteins and to influence alternative splicing in overexpression systems. Here we used endogenous CLK2 protein to demonstrate that it displays different biochemical characteristics compared with its overexpressed protein and that it is differentially phosphorylated in vivo. Furthermore, CLK2 changed its nuclear localization upon treatment with the **kinase** inhibitor 5, 6-dichloro-1-beta-D-ribofuranosylbenzimidazole. We have also identified a CLK2 autophosphorylation site, which is highly conserved among all CLK proteins, and we show by site-directed mutagenesis that its phosphorylation influences the subnuclear localization of CLK2. Our data suggest that CLK2 localization and possibly activity are influenced by a balance of CLK2 autophosphorylation and the regulation by CLK2 **kinases** and phosphatases.

L8 ANSWER 12 OF 78 MEDLINE on STN
ACCESSION NUMBER: 1998352108 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9685421
TITLE: A **serine/arginine-rich** domain in the **human** U1 70k protein is necessary and sufficient for ASF/SF2 binding.
AUTHOR: Cao W; Garcia-Blanco M A
CORPORATE SOURCE: Department of Pharmacology and Cancer Biology, Levine Science Research Center, Duke University Medical Center, Durham, North Carolina 27710, USA.
SOURCE: Journal of biological chemistry, (1998 Aug 7) 273 (32) 20629-35.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980917
Last Updated on STN: 20020420
Entered Medline: 19980910

AB Critical protein-protein interactions among pre-mRNA splicing factors determine splicing efficiency and specificity. The **serine/arginine** proteins, a family of factors characterized by the presence of an RNA recognition motif and an arginine/serine domain, are essential for constitutive splicing and required for some alternative splicing decisions. ASF/SF2, SC35, and other members of the **serine/arginine** family, interact with the 70k protein of the U1 small nuclear ribonucleoprotein. The binding of this protein with ASF/SF2 is thought to enhance recognition of the 5' splice site of pre-mRNAs by the U1 small nuclear ribonucleoprotein. It has been clearly documented that the arginine/serine domain of ASF/SF2 is responsible for binding to the U1 70k protein. In this manuscript we characterize the segment in the **human** U1 70k protein that is both necessary and sufficient for ASF/SF2 binding. A domain within this segment, which begins with Arg240 and ends with Asp270, was shown to bind specifically to the arginine/serine domain of ASF/SF2 using a yeast two-hybrid system and a far Western assay. Mutational analysis of this segment suggested that several arginines are critical for the interaction with ASF/SF2 and for phosphorylation by SRPK1. Inspection of the sequence of the Arg248 to Asp270 region suggested this as an arginine/serine-like domain in U1 70k protein, and the data presented in this manuscript strongly support this view. Inspection of the **human** U1 70k protein sequence, comparison with homologues in other animal species, and mutational analysis indicated the importance of the sequence Arg-Arg-Arg-Ser-Arg-Ser-Arg-Asp, which is found repeated twice in the region from Arg248 to Asp270 in the **human** protein.

L8 ANSWER 13 OF 78 MEDLINE on STN
ACCESSION NUMBER: 1998088885 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9428609
TITLE: DNA topoisomerase I: customs officer at the border between DNA and RNA worlds?.
AUTHOR: Tazi J; Rossi F; Labourier E; Gallouzi I; Brunel C; Antoine E
CORPORATE SOURCE: Institut de Genetique Moleculaire de Montpellier, UMR 5535 CNRS, Universite de Montpellier II, France.
SOURCE: Journal of molecular medicine (Berlin, Germany), (1997 Nov-Dec) 75 (11-12) 786-800. Ref: 226
Journal code: 9504370. ISSN: 0946-2716.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980224
Last Updated on STN: 19980224
Entered Medline: 19980209

AB DNA topoisomerase I is required for the normal development of multicellular organisms, probably because it plays a role in controlling gene activity, in addition to its function in relieving tortional stress during DNA replication and transcription. The discovery of DNA topoisomerase I as a specific **kinase** that phosphorylates **serine-arginine rich** (SR) splicing factors may provide new insights into their precise function in regulating gene **expression**. It is clear that the splicing factors phosphorylated by DNA topoisomerase I can modulate gene **expression** by changing the splicing pattern of structural genes. Studies of the splicing mechanism suggest that the phosphorylation of serine residues of SR proteins contribute to their activity. As this phosphorylation can be accomplished by several **kinases**, it remains to be determined whether phosphorylation by DNA topoisomerase I protein **kinase** is the limiting step in regulating this process. The availability of specific inhibitors of DNA topoisomerase I, structurally related to the alkaloid camptothecin, have made it possible to address this question experimentally. These inhibitors, which hold great promise as antineoplastic drugs, lead to specific inhibition of SR protein phosphorylation in cultured cells. This observation will hopefully lead to improved understanding of the mechanism by which these drugs act at cellular level.

L8 ANSWER 14 OF 78 MEDLINE on STN
ACCESSION NUMBER: 96394614 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8798720
TITLE: SRPK1 and Clk/Sty protein **kinases** show distinct substrate specificities for **serine/arginine-rich** splicing factors.
AUTHOR: Colwill K; Feng L L; Yeakley J M; Gish G D; Caceres J F; Pawson T; Fu X D
CORPORATE SOURCE: Programme in Molecular Biology and Cancer, Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, Ontario M5G 1X5, Canada.
SOURCE: Journal of biological chemistry, (1996 Oct 4) 271 (40) 24569-75.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 20020420
Entered Medline: 19961125

AB **Serine/arginine-rich** (SR) proteins are essential for pre-mRNA splicing, and modify the choice of splice site during alternative splicing in a process apparently regulated by protein phosphorylation. Two protein **kinases** have been **cloned** that can phosphorylate SR proteins in vitro: SRPK1 and Clk/Sty. Here, we show that these two **kinases** phosphorylate the same SR proteins in vitro, but that SRPK1 has the higher specific activity toward ASF/SF2. SRPK1, like Clk/Sty, phosphorylates ASF/SF2 in vitro on sites that are also phosphorylated in vivo. Tryptic peptide mapping of ASF/SF2 revealed that three of the phosphopeptides from full-length ASF/SF2 phosphorylated in vitro contain consecutive phosphoserine-arginine residues or

phosphoserine-proline residues. In vitro, the Clk/Sty **kinase** phosphorylated Ser-Arg, Ser-Lys, or Ser-Pro sites, whereas SRPK1 had a strong preference for Ser-Arg sites. These results suggest that SRPK1 and Clk/Sty may play different roles in regulating SR splicing factors, and suggest that Clk/Sty has a broader substrate specificity than SRPK1.

L8 ANSWER 15 OF 78 MEDLINE on STN
ACCESSION NUMBER: 95372342 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7644475
TITLE: Identification of a plant **serine-arginine -rich** protein similar to the mammalian splicing factor SF2/ASF.
AUTHOR: Lazar G; Schaal T; Maniatis T; Goodman H M
CORPORATE SOURCE: Department of Molecular Biology, Massachusetts General Hospital, Boston 02114, USA.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1995 Aug 15) 92 (17) 7672-6. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-M98340
ENTRY MONTH: 199509
ENTRY DATE: Entered STN: 19950930
Last Updated on STN: 19950930
Entered Medline: 19950921

AB We show that the higher plant Arabidopsis thaliana has a **serine-arginine-rich** (SR) protein family whose members contain a phosphoepitope shared by the animal SR family of splicing factors. In addition, we report the **cloning** and characterization of a cDNA encoding a higher-plant SR protein from Arabidopsis, SR1, which has striking sequence and structural homology to the **human** splicing factor SF2/ASF. Similar to SF2/ASF, the plant SR1 protein promotes splice site switching in mammalian nuclear extracts. A novel feature of the Arabidopsis SR protein is a C-terminal domain containing a high concentration of proline, serine, and lysine residues (PSK domain), a composition reminiscent of histones. This domain includes a putative phosphorylation site for the mitotic **kinase** cyclin/p34cdc2.

L8 ANSWER 16 OF 78 MEDLINE on STN
ACCESSION NUMBER: 94268559 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8208298
TITLE: A serine **kinase** regulates intracellular localization of splicing factors in the cell cycle.
COMMENT: Comment in: Nature. 1994 Jun 23;369(6482):604. PubMed ID: 8208284
AUTHOR: Gui J F; Lane W S; Fu X D
CORPORATE SOURCE: Division of Cellular and Molecular Medicine, University of California at San Diego 92093-0651.
SOURCE: Nature, (1994 Jun 23) 369 (6482) 678-82. Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-M13447; GENBANK-S28282; GENBANK-U09564
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 19940721
Last Updated on STN: 20020420
Entered Medline: 19940714

AB Small nuclear ribonucleoprotein particles (snRNPs) and non-snRNP splicing factors containing a **serine/arginine-rich**

domain (SR proteins) concentrate in 'speckles' in the nucleus of interphase cells. It is believed that nuclear speckles act as storage sites for splicing factors while splicing occurs on nascent transcripts. Splicing factors redistribute in response to transcription inhibition or viral infection, and nuclear speckles break down and reform as cells progress through mitosis. We have now identified and **cloned** a **kinase**, SRPK1, which is regulated by the cell cycle and is specific for SR proteins; this **kinase** is related to a Caenorhabditis elegans **kinase** and to the fission yeast **kinase** Dsk1 (reference 7). SRPK1 specifically induces the disassembly of nuclear speckles, and a high level of SRPK1 inhibits splicing in vitro. Our results indicate that SRPK1 may have a central role in the regulatory network for splicing, controlling the intranuclear distribution of splicing factors in interphase cells, and the reorganization of nuclear speckles during mitosis.

L8 ANSWER 17 OF 78 EMBASE
on STN

ACCESSION NUMBER: 2004304515 EMBASE
TITLE: Resistance to platinum-containing chemotherapy in testicular germ cell tumors is associated with downregulation of the protein **kinase** SRPK1.
AUTHOR: Schenk P.W.; Stoop H.; Bokemeyer C.; Mayer F.; Stoter G.; Oosterhuis J.W.; Wiemer E.; Looijenga L.H.J.; Nooter K.
CORPORATE SOURCE: Dr. K. Nooter, Lab. Translational/Molec. Pharmacol., Department of Medical Oncology, Josephine Nefkens Institute Be422, PO Box 1738, Rotterdam 3000 DR, Netherlands. k.nooter@erasmusmc.nl
SOURCE: Neoplasia, (2004) 6/4 (297-301).
Refs: 20
ISSN: 1522-8002 CODEN: NEOPFL
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
022 Human Genetics
028 Urology and Nephrology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Male germ cell tumors (GCTs) are extremely sensitive to platinum-containing chemotherapy, with only 10% of patients showing therapy resistance. However, the biological basis of the high curability of disseminated GCTs by chemotherapy is still unknown. Recently, we demonstrated that the mammalian **serine/arginine-rich** protein-specific **kinase** 1 (SRPK1) is a cisplatin-sensitive gene, inactivation of which leads to cisplatin resistance. Because, in mammalians, the **expression** of SRPK1 is preferentially high in testicular tissues, cisplatin responsiveness of male GCTs might be associated with SRPK1 levels. In the present study, we monitored SRPK1 protein **expression** in a unique series of nonseminomatous GCTs by immunohistochemistry. Randomly selected GCTs (n = 70) and tumors from patients responding to standard chemotherapy (n = 20) generally showed strong SRPK1 staining. In contrast, **expression** in refractory GCTs (n = 20) as well as in GCTs from poor-prognosis patients responding to high-dose chemotherapy only (n = 11) was significantly lower (two-sided Wilcoxon rank sum test: P < .001). In conclusion, our data suggest that SRPK1 **expression** might be an important prognostic indicator for the chemoresponsiveness of nonseminomatous GCTs.

L8 ANSWER 18 OF 78 EMBASE
on STN

ACCESSION NUMBER: 2004243883 EMBASE

TITLE: Manipulation of alternative splicing by a newly developed inhibitor of Clks.

AUTHOR: Muraki M.; Ohkawara B.; Hosoya T.; Onogi H.; Koizumi J.; Koizumi T.; Sumi K.; Yomoda J.-I.; Murray M.V.; Kimura H.; Furuichi K.; Shibuya H.; Krainer A.R.; Suzuki M.; Hagiwara M.

CORPORATE SOURCE: M. Hagiwara, Laboratory of Gene Expression, School of Biomedical Science, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8510, Japan. m.hagiwara.end@mri.tmd.ac.jp

SOURCE: Journal of Biological Chemistry, (4 Jun 2004) 279/23 (24246-24254).
Refs: 59
ISSN: 0021-9258 CODEN: JBCHA3

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The regulation of splice site usage provides a versatile mechanism for controlling gene **expression** and for the generation of proteome diversity, playing an essential role in many biological processes. The importance of alternative splicing is further illustrated by the increasing number of **human** diseases that have been attributed to mis-splicing events. Appropriate spatial and temporal generation of splicing variants demands that alternative splicing be subjected to extensive regulation, similar to transcriptional control. The Clk (Cdc2-like **kinase**) family has been implicated in splicing control and consists of at least four members. Through extensive screening of a chemical library, we found that a benzothiazole compound, TG003, had a potent inhibitory effect on the activity of Clk1/Sty. TG003 inhibited SF2/ASF-dependent splicing of β-globin pre-mRNA in vitro by suppression of Clk-mediated phosphorylation. This drug also suppressed **serine/arginine-rich** protein phosphorylation, dissociation of nuclear speckles, and Clk1/Sty-dependent alternative splicing in mammalian cells. Consistently, administration of TG003 rescued the embryonic defects induced by excessive Clk activity in Xenopus. Thus, TG003, a novel inhibitor of Clk family will be a valuable tool to dissect the regulatory mechanisms involving **serine/arginine-rich** protein phosphorylation signaling pathways in vivo, and may be applicable for the therapeutic manipulation of abnormal splicing.

L8 ANSWER 19 OF 78 EMBASE on STN

ACCESSION NUMBER: 2003457750 EMBASE

TITLE: **Cloning** of **Human** PRP4 Reveals Interaction with Clk1.

AUTHOR: Kojima T.; Zama T.; Wada K.; Onogi H.; Hagiwara M.

CORPORATE SOURCE: M. Hagiwara, Department of Functional Genomics, Medical Research Institute, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8510, Japan. m.hagiwara.end@mri.tmd.ac.jp

SOURCE: Journal of Biological Chemistry, (24 Aug 2001) 276/34 (32247-32256).
Refs: 48
ISSN: 0021-9258 CODEN: JBCHA3

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Prp4 is a protein **kinase** of Schizosaccharomyces pombe identified

through its role in pre-mRNA splicing, and belongs to a **kinase** family including mammalian **serine/arginine-rich** protein-specific **kinases** and Clks, whose substrates are **serine/arginine-rich** proteins. We **cloned human** PRP4 (hPRP4) full-length cDNA and the antiserum raised against a partial peptide of hPRP4 recognized 170-kDa polypeptide in HeLa S3 cell extracts. Northern blot analysis revealed that hPRP4 mRNA was ubiquitously **expressed** in multiple tissues. The extended NH(2)-terminal region of hPRP4 contains an arginine/serine-rich domain and putative nuclear localization signals. hPRP4 phosphorylated and interacted with SF2/ASF, one of the essential splicing factors. Indirect immunofluorescence analysis revealed that endogenous hPRP4 was distributed in a nuclear speckled pattern and colocalized with SF2/ASF in HeLa S3 cells. Furthermore, hPRP4 interacted directly with Clk1 on its COOH terminus, and the arginine/serine-rich domain of hPRP4 was phosphorylated by Clk1 in vitro. Overexpression of Clk1 caused redistribution of hPRP4, from the speckled to the diffuse pattern in nucleoplasm, whereas inactive mutant of Clk1 caused no change of hPRP4 localization. These findings suggest that the NH (2)-terminal region of hPRP4 may play regulatory roles under an unidentified signal transduction pathway through Clk1.

L8 ANSWER 20 OF 78 EMBASE
on STN

ACCESSION NUMBER: 2003425967 EMBASE
TITLE: Monochloramine induces reorganization of nuclear speckles and phosphorylation of SRp30 in **human** colonic epithelial cells: Role of protein **kinase** C.
AUTHOR: Zhu Y.-Q.; Lu Y.; Tan X.-D.
CORPORATE SOURCE: X.-D. Tan, Disease Pathogenesis Program, Children's Mem. Inst. for Educ./Res., Children's Memorial Hospital, 2300 Children's Plaza, Chicago, IL 60614, United States. xtan@northwestern.edu
SOURCE: American Journal of Physiology - Cell Physiology, (2003) 285/5 54-5 (C1294-C1303).
Refs: 66
ISSN: 0363-6143 CODEN: AJPCDD
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Intestinal epithelial cells are constantly stimulated by reactive oxidant metabolites (ROMs) in inflamed mucosa. Monochloramine (NH(2)Cl), a cell-permeant ROM, is particularly relevant to the pathogenesis of inflammation in the gastrointestinal tract. Nuclear speckles, a unique nuclear subcompartment, accumulate a family of proteins, namely, serine- and arginine-rich (SR) proteins. They play important roles in regulation of pre-mRNA splicing. Currently, little is known about the link between inflammatory stimulation and the pre-mRNA splicing process, although gene **expression** is changed in inflamed tissues. The present study was designed to investigate whether stimulation of **human** colonic epithelial cells (HT-29 and Caco-2 cell lines) with NH(2)Cl affects nuclear speckles and their components. By indirect immunofluorescence, nuclear speckles have been shown to undergo rapid aggregation after NH(2)Cl stimulation. By utilizing Western blotting, SRp30 (a subset of SR proteins) in intestinal epithelial cells was found to be phosphorylated after NH(2)Cl treatment, whereas other SR proteins were not responsive to NH(2)Cl stimulation. The cytotoxic effect of NH(2)Cl was excluded by both negative lactate dehydrogenase assay and propidium iodide staining. Therefore, NH (2)Cl-induced morphological changes on nuclear speckles and phosphorylated SRp30 do not result from intestinal epithelial injury. Furthermore, the effect of NH(2)Cl on nuclear speckles and SRp30 was

blocked by bisindolylmaleimide I, a selective PKC inhibitor. Together, the available data suggest that stimulation of intestinal epithelial cells with NH(2)Cl results in a consequent change on pre-mRNA splicing machinery via a distinctive signal pathway involving activation of PKC. This effect may contribute to oxidant-induced pathophysiological changes in the gastrointestinal tract.

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ACCESSION NUMBER: 2003225957 EMBASE
TITLE: Cell differentiation of gonadotropin-releasing hormone neurons and alternative RNA splicing of the gonadotropin-releasing hormone transcript.
AUTHOR: Choe Y.; Son G.H.; Lee S.; Park E.; Moon Y.; Kim K.
CORPORATE SOURCE: K. Kim, School of Biological Sciences, Seoul National University, Seoul 151-742, Korea, Republic of. kyungjin@snu.ac.kr
SOURCE: Neuroendocrinology, (2003) 77/4 (282-290).
Refs: 55
ISSN: 0028-3835 CODEN: NUNDAJ
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
008 Neurology and Neurosurgery
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Two different, yet related issues regarding gonadotropin-releasing hormone (GnRH), i.e. the development and differentiation of hypothalamic GnRH neurons and the alternative RNA splicing of GnRH gene transcripts, are addressed in the present review. Using the immortalized GnRH-producing GT1 cell line, we found that activation of protein **kinase** C (PKC) with 12-O-tetradecanoylphorbol-13-acetate induces morphological and functional differentiation of these neurons. Specific isoforms of PKC are involved in neurite growth, cell migration and synaptic contacts and involve different signaling pathways. Using an in vitro splicing assay with HeLa nuclear extract, we found that excision of the first intron of the GnRH primary transcript is attenuated in non-GnRH-producing cells, but not in GnRH-producing cells such as GT1. This attenuation was relieved by exonic splicing enhancers located in the GnRH exons 3 and 4. Interestingly, addition of nuclear extract derived from GT1 cells further increased the excision rate of intron A, indicating that GnRH neurons contain trans-acting splicing factors. Extensive biochemical analysis indicates that Tra2α, a **serine/arginine-rich** RNA-binding protein, and other cofactors are likely involved in mediating neuron-specific excision of intron A from the GnRH primary transcript. An understanding of the GnRH neuron-specific splicing machinery provides critical insight into the molecular mechanism of GnRH gene regulation and consequently of mammalian reproductive development.

L8 ANSWER 22 OF 78 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003201086 EMBASE
TITLE: Differential effects of hyperphosphorylation on splicing factor SRp55.
AUTHOR: Lai M.-C.; Lin R.-I.; Tarn W.-Y.
CORPORATE SOURCE: W.-Y. Tarn, Institute of Biomedical Sciences, Academia Sinica, 128 Academy Road Section 2, Nankang, Taipei 11529, Taiwan,Province of China. wtarn@ibms.sinica.edu.tw
SOURCE: Biochemical Journal, (1 May 2003) 371/3 (937-945).
Refs: 43
ISSN: 0264-6021 CODEN: BIJOAK

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Members of the **serine/arginine-rich** (SR) protein family play an important role in both constitutive and regulated splicing of precursor mRNAs. Phosphorylation of the arginine/serine dipeptide-rich domain (RS domain) can modulate the activity and the subcellular localization of SR proteins. However, whether the SR protein family members are individually regulated and how this is achieved remain unclear. In this report we show that 5,6-dichloro-1β-D-ribofuranosyl-benzimidazole (DRB), an inhibitor of RNA polymerase II-dependent transcription, specifically induced hyperphosphorylation of SRp55 but not that of any other SR proteins tested. Hyperphosphorylation of SRp55 occurs at the RS domain and appears to require the RNA-binding activity. Upon DRB treatment, hyperphosphorylated SRp55 relocates to enlarged nuclear speckles. Intriguingly, SRp55 is specifically targeted for degradation by the proteasome upon overexpression of the SR protein **kinase** Clk/Sty. Although a destabilization signal is mapped within the C-terminal 43-amino acid segment of SRp55, its adjacent lysine/serine-rich RS domain is nevertheless critical for the Clk/Sty-mediated degradation. We report for the first time that SRp55 can be hyperphosphorylated under different circumstances whereby its fate is differentially influenced.

L8 ANSWER 23 OF 78 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003095816 EMBASE
TITLE: An early ancestor in the evolution of splicing: A Trypanosoma cruzi **serine-arginine-rich** protein (TcSR) is functional in cis-splicing.
AUTHOR: Portal D.; Espinosa J.M.; Lobo G.S.; Kadener S.; Pereira C.A.; De La Mata M.; Tang Z.; Lin R.-J.; Kornblihtt A.R.; Baralle F.E.; Flawia M.M.; Torres H.N.
CORPORATE SOURCE: H.N. Torres, Fac. de Ciencias Exactas y Naturales, Inst. Invest. Ing. Genet. Biol. M., Universidad de Buenos Aires, Buenos Aires, Argentina. torres@proteus.dna.uba.ar
SOURCE: Molecular and Biochemical Parasitology, (2003) 127/1 (37-46).
Refs: 58
ISSN: 0166-6851 CODEN: MBIPDP
PUBLISHER IDENT.: S 0166-6851(02)00301-8
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB A novel **serine-arginine-rich** protein designated TcSR was identified in Trypanosoma cruzi. The deduced amino acid sequence reveals that TcSR is a member of the SR protein family of splicing factors that contains two RNA-binding domains at the N-terminal side and several **serine-arginine** repeats at the COOH-terminus. Over **expression** of either TcSR or the **human** SR-protein associated splicing factor/splicing factor 2 (ASF/SF2) in wild-type Schizosaccharomyces pombe, provoked an elongated phenotype similar to that of fission yeast over **expressing** the SR-containing splicing factor Prp2, a U2AF(65) orthologue. When a double mutant strain lacking two SR protein-specific protein **kinases** was used, **expression** of TcSR or **human** SR ASF/SF2 splicing factor reverted the mutant to a wild-type phenotype. Transient **expression** of TcSR in HeLa cells stimulated the inclusion of the EDI exon of **human** fibronectin in an in vivo functional alternative cis-splicing assay. Inclusion was dependent on a splicing

enhancer sequence present in the EDI exon. In addition, TcSR and peptides carrying TcSR-RS domain sequences were phosphorylated by a **human** SR protein **kinase**. These results indicate that TcSR is a member of the SR splicing network and that some components common to the trans- and cis-splicing machineries evolved from the early origins of the eukaryotic lineage. .COPYRGT. 2002 Elsevier Science B.V. All rights reserved.

L8 ANSWER 24 OF 78 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003039358 EMBASE
TITLE: Exonic splicing enhancer-dependent selection of the bovine papillomavirus type 1 nucleotide 3225 3' splice site can be rescued in a cell lacking splicing factor ASF/SF2 through activation of the phosphatidylinositol 3-**kinase** /Akt pathway.
AUTHOR: Liu X.; Mayeda A.; Tao M.; Zheng Z.-M.
CORPORATE SOURCE: Z.-M. Zheng, HIV and AIDS Malignancy Branch, Center for Cancer Research, NCI/NIH, 10 Center Dr., Bethesda, MD 20892-1868, United States. zhengt@exchange.nih.gov
SOURCE: Journal of Virology, (2003) 77/3 (2105-2115).
Refs: 60
ISSN: 0022-538X CODEN: JOVIAM
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Bovine papillomavirus type 1 (BPV-1) late pre-mRNAs are spliced in keratinocytes in a differentiation-specific manner: the late leader 5' splice site alternatively splices to a proximal 3' splice site (at nucleotide 3225) to **express** L2 or to a distal 3' splice site (at nucleotide 3605) to **express** L1. Two exonic splicing enhancers, each containing two ASF/SF2 (alternative splicing factor/splicing factor 2) binding sites, are located between the two 3' splice sites and have been identified as regulating alternative 3' splice site usage. The present report demonstrates for the first time that ASF/SF2 is required under physiological conditions for the **expression** of BPV-1 late RNAs and for selection of the proximal 3' splice site for BPV-1 RNA splicing in DT40-ASF cells, a genetically engineered chicken B-cell line that **expresses** only **human** ASF/SF2 controlled by a tetracycline-repressible promoter. Depletion of ASF/SF2 from the cells by tetracycline greatly decreased viral RNA **expression** and RNA splicing at the proximal 3' splice site while increasing use of the distal 3' splice site in the remaining viral RNAs. Activation of cells lacking ASF/SF2 through anti-immunoglobulin M-B-cell receptor cross-linking rescued viral RNA **expression** and splicing at the proximal 3' splice site and enhanced Akt phosphorylation and **expression** of the phosphorylated **serine/arginine-rich** (SR) proteins SRp30s (especially SC35) and SRp40. Treatment with wortmannin, a specific phosphatidylinositol 3-**kinase**/Akt **kinase** inhibitor, completely blocked the activation-induced activities. ASF/SF2 thus plays an important role in viral RNA **expression** and splicing at the proximal 3' splice site, but activation-rescued viral RNA **expression** and splicing in ASF/SF2-depleted cells is mediated through the phosphatidylinositol 3-**kinase**/Akt pathway and is associated with the enhanced **expression** of other SR proteins.

L8 ANSWER 25 OF 78 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003011795 EMBASE
TITLE: PSKH1, a novel splice factor compartment-associated serine **kinase**.

AUTHOR: Brede G.; Solheim J.; Prydz H.
CORPORATE SOURCE: H. Prydz, Biotechnology Centre of Oslo, University of Oslo, Gaustadalleen 21, N-0349 Oslo, Norway. hans.prydz@biotek.uio.no
SOURCE: Nucleic Acids Research, (1 Dec 2002) 30/23 (5301-5309). Refs: 40
ISSN: 0305-1048 CODEN: NARHAD
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Small nuclear ribonucleoprotein particles (snRNPs) and non-snRNP splicing factors containing a **serine/arginine-rich** domain (SR proteins) concentrate in splicing factor compartments (SFCs) within the nucleus of interphase cells. Nuclear SFCs are considered mainly as storage sites for splicing factors, supplying splicing factors to active genes. The mechanisms controlling the interaction of the various spliceosome constituents, and the dynamic nature of the SFCs, are still poorly understood. We show here that endogenous PSKH1, a previously **cloned kinase**, is located in SFCs. Migration of PSKH1-FLAG into SFCs is enhanced during co-**expression** of T7-tagged ASF/SF2 as well as other members of the SR protein family, but not by two other non-SR nuclear proteins serving as controls. Similar to the SR protein **kinase** family, overexpression of PSKH1 led to reorganization of co-**expressed** T7-SC35 and T7-ASF/SF2 into a more diffuse nuclear pattern. This redistribution was not dependent on PSKH1 **kinase** activity. Different from the SR protein **kinases**, the SFC-associating features of PSKH1 were located within its catalytic **kinase** domain and within its C-terminus. Although no direct interaction was observed between PSKH1 and any of the SR proteins tested in pull-down or yeast two-hybrid assays, forced **expression** of PSKH1-FLAG was shown to stimulate distal splicing of an E1A mini-gene in HeLa cells. Moreover, a GST-ASF/SF2 fusion was not phosphorylated by PSKH1, suggesting an indirect mechanism of action on SR proteins. Our data suggest a mutual relationship between PSKH1 and SR proteins, as they are able to target PSKH1 into SFCs, while forced PSKH1 **expression** modulates nuclear dynamics and the function of co-**expressed** splicing factors.

L8 ANSWER 26 OF 78 EMBASE on STN
ACCESSION NUMBER: 2001357193 EMBASE
TITLE: SKY1 is involved in cisplatin-induced cell kill in Saccharomyces cerevisiae, and inactivation of its **human** homologue, SRPK1, induces cisplatin resistance in a **human** ovarian carcinoma cell line.
AUTHOR: Schenk P.W.; Boersma A.W.M.; Brandsma J.A.; Den Dulk H.; Burger H.; Stoter G.; Brouwer J.; Nooter K.
CORPORATE SOURCE: K. Nooter, Department of Medical Oncology, University Hospital Rotterdam, Josephine Nefkens Building, P. O. Box 1738, 3000 DR Rotterdam, Netherlands. nooter@oncd.azr.nl
SOURCE: Cancer Research, (1 Oct 2001) 61/19 (6982-6986). Refs: 23
ISSN: 0008-5472 CODEN: CNREA8
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 010 Obstetrics and Gynecology
016 Cancer
030 Pharmacology
037 Drug Literature Index

LANGUAGE: English
SUMMARY LANGUAGE: English
AB The therapeutic potential of cisplatin, one of the most active and widely used anticancer drugs, is severely limited by the occurrence of cellular resistance. In this study, using budding yeast Saccharomyces cerevisiae as a model organism to identify novel drug resistance genes, we found that disruption of the yeast gene SKY1 (**serine/arginine-rich** protein-specific **kinase** from budding yeast) by either transposon insertion or one-step gene replacement conferred cellular resistance to cisplatin. Heterologous **expression** of the **human** SKY1 homologue SRPK1 (**serine/arginine-rich** protein-specific **kinase**) in SKY1 deletion mutant yeast cells restored cisplatin sensitivity, suggesting that SRPK1 is a cisplatin sensitivity gene, the inactivation of which could lead to cisplatin resistance. Subsequently, we investigated the role of SRPK1 in cisplatin sensitivity and resistance in **human** ovarian carcinoma A2780 cells using antisense oligodeoxynucleotides. Treatment of A2780 cells with antisense oligodeoxynucleotides directed against the translation initiation site of SRPK1 led to down-regulation of SRPK1 protein and conferred a 4-fold resistance to cisplatin. The **human** SRPK1 gene has not been associated with drug resistance before. Our new findings strongly suggest that SRPK1 is involved in cisplatin-induced cell kill and indicate that SRPK1 might potentially be of importance for studying clinical drug resistance.

L8 ANSWER 27 OF 78 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 97370687 EMBASE
DOCUMENT NUMBER: 1997370687
TITLE: DNA topoisomerase I: Customs officer at the border between DNA and RNA worlds?.
AUTHOR: Tazi J.; Rossi F.; Labourier E.; Gallouzi I.-E.; Brunel C.; Antoine E.
CORPORATE SOURCE: Dr. J. Tazi, Inst. Genetique Molecul. Montpellier, UMR 5535 CNRS, Universite de Montpellier II, 1919 Route de Mende, F-34033 Montpellier Cedex 1, France
SOURCE: Journal of Molecular Medicine, (1997) 75/11-12 (786-800). Refs: 226
ISSN: 0946-2716 CODEN: JMLME8
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
021 Developmental Biology and Teratology
022 Human Genetics
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB DNA topoisomerase I is required for the normal development of multicellular organisms, probably because it plays a role in controlling gene activity, in addition to its function in relieving tortional stress during DNA replication and transcription. The discovery of DNA topoisomerase I as a specific **kinase** that phosphorylates **serine-arginine rich** (SR) splicing factors may provide new insights into their precise function in regulating gene **expression**. It is clear that the splicing factors phosphorylated by DNA topoisomerase I can modulate gene **expression** by changing the splicing pattern of structural genes. Studies of the splicing mechanism suggest that the phosphorylation of serine residues of SR proteins contribute to their activity. As this phosphorylation can be accomplished by several **kinases**, it remains to be determined whether phosphorylation by DNA topoisomerase I protein **kinase** is the limiting step in regulating this process. The availability of specific

inhibitors of DNA topoisomerase I, structurally related to the alkaloid camptothecin, have made it possible to address this question experimentally. These inhibitors, which hold great promise as antineoplastic drugs, lead to specific inhibition of SR protein phosphorylation in cultured cells. This observation will hopefully lead to improved understanding of the mechanism by which these drugs act at cellular level.

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ACCESSION NUMBER: 95256030 EMBASE
DOCUMENT NUMBER: 1995256030
TITLE: Identification of a plant **serine-arginine -rich** protein similar to the mammalian splicing factor SF2/ASF.
AUTHOR: Lazar G.; Schaal T.; Maniatis T.; Goodman H.M.
CORPORATE SOURCE: Department of Molecular Biology, Wellman Building 11, Massachusetts General Hospital, 50 Blossom Street,Boston, MA 02114, United States
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1995) 92/17 (7672-7676). ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB We show that the higher plant Arabidopsis thaliana has a **serine-arginine- rich** (SR) protein family whose members contain a phosphoepitope shared by the animal SR family of splicing factors. In addition, we report the **cloning** and characterization of a cDNA encoding n higher-plant SR protein from Arabidopsis, SR1, which has striking sequence and structural homology to the **human** splicing factor SF2/ASF. Similar to SF2/ASF, the plant SR1 protein promotes splice site switching in mammalian nuclear extracts. A novel feature of the Arabidopsis SR protein is a C-terminal domain containing a high concentration of proline, serine, and lysine residues (PSK domain), a composition reminiscent of histones. This domain includes a putative phosphorylation site for the mitotic **kinase** cyclin/p34(cdc2).

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ACCESSION NUMBER: 94200154 EMBASE
DOCUMENT NUMBER: 1994200154
TITLE: A serine **kinase** regulates intracellular localization of splicing factors in the cell cycle.
AUTHOR: Gui J.-F.; Lane W.S.; Fu X.-D.
CORPORATE SOURCE: Div. of Cellular/Molecular Medicine, University of California, San Diego, 9500 Gilman Drive,La Jolla, CA 92093-0651, United States
SOURCE: Nature, (1994) 369/6482 (678-682). ISSN: 0028-0836 CODEN: NATUAS
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Small nuclear ribonucleoprotein particles (snRNPs) and non-snRNP splicing factors containing a **serine/arginine-rich** domain (SR proteins) concentrate in 'speckles' in the nucleus of interphaae cells. It is believed that nuclear speckles act as storage sites for splicing factors while splicing occurs on nascent transcripts. Splicing factors redistribute in response to transcription inhibition or

viral infection, aud nuclear speckles break down and reform as cells progress through mitosis. We have now identified and **cloned** a **kinase**, SRPK1, which is regulated by the cell cycle and is specific for SR proteins; this **kinase** is related to a Caenorhabditis elegans **kinase** and to the fission yeast **kinase** Dsk1. SRPK1 specifically induces the disassembly of nuclear speckles, and a high level of SRPK1 inhibits splicing in vitro. Our results indicate that SRPK1 may have a central role in the regulatory network for splicing, controlling the intranuclear distribution of splicing factors in interphase cells, and the reorganization of nuclear speckles during mitosis.

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ACCESSION NUMBER: 2004:401559 BIOSIS
DOCUMENT NUMBER: PREV200400398274
TITLE: Resistance to platinum-containing chemotherapy in testicular germ cell tumors is associated with downregulation of the protein **kinase** SRPK1.
AUTHOR(S): Schenk, Paul W.; Stoop, Hans; Bokemeyer, Carsten; Mayer, Frank; Stoter, Gerrit; Oosterhuis, J. Wolter; Wiemer, Erik; Looijenga, Leendert H. J.; Nooter, Kees [Reprint Author]
CORPORATE SOURCE: Med CtrDept Med OncolLab Translat and Mol Pharmacol,Josephine Nefkens In, Erasmus Univ, Be422,POB 1738, NL-3000 DR, Rotterdam, Netherlands k.nooter@erasmusmc.nl
SOURCE: Neoplasia (New York), (July 2004) Vol. 6, No. 4, pp. 297-301. print.
ISSN: 1522-8002.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Oct 2004
Last Updated on STN: 13 Oct 2004

AB Male germ cell tumors (GCTs) are extremely sensitive to platinum-containing chemotherapy, with only 10% of patients showing therapy resistance. However, the biological basis of the high curability of disseminated GCTs by chemotherapy is still unknown. Recently, we demonstrated that the mammalian **serine/arginine-rich** protein-specific **kinase** 1 (SRPK1) is a cisplatin-sensitive gene, inactivation of which leads to cisplatin resistance. Because, in mammalians, the **expression** of SRPK1 is preferentially high in testicular tissues, cisplatin responsiveness of male GCTs might be associated with SRPK1 levels. In the present study, we monitored SRPK1 protein **expression** in a unique series of nonseminomatous GCTs by immunohistochemistry. Randomly selected GCTs (n = 70) and tumors from patients responding to standard chemotherapy (n = 20) generally showed strong SRPK1 staining. In contrast, **expression** in refractory GCTs (n = 20) as well as in GCTs from poor-prognosis patients responding to high-dose chemotherapy only (n = 11) was significantly lower (two-sided Wilcoxon rank sum test: $P < .001$). In conclusion, our data suggest that SRPK1 **expression** might be an important prognostic indicator for the chemoresponsiveness of nonseminomatous GCTs.

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ACCESSION NUMBER: 2004:316263 BIOSIS
DOCUMENT NUMBER: PREV200400315861
TITLE: Manipulation of alternative splicing by a newly developed inhibitor of Clks.
AUTHOR(S): Muraki, Michiko; Ohkawara, Bisei; Hosoya, Takamitsu; Onogi, Hiroshi; Koizumi, Jun; Koizumi, Tomonobu; Sumi, Kengo; Yomoda, Jun-ichiro; Murray, Michael V.; Kimura, Hiroshi;

Furuichi, Kiyoshi; Shibuya, Hiroshi; Krainer, Adrian R.; Suzuki, Masaaki; Hagiwara, Masatoshi [Reprint Author]

CORPORATE SOURCE: Sch Biomed SciGene Express LabBunkyo Ku, Tokyo Med and Dent Univ, 1-5-45 Yushima, Tokyo, 1138510, Japan
m.hagiwara.end@mri.tmd.ac.jp

SOURCE: Journal of Biological Chemistry, (June 4 2004) Vol. 279, No. 23, pp. 24246-24254. print.
CODEN: JBCHA3. ISSN: 0021-9258.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Jul 2004
Last Updated on STN: 15 Jul 2004

AB The regulation of splice site usage provides a versatile mechanism for controlling gene **expression** and for the generation of proteome diversity, playing an essential role in many biological processes. The importance of alternative splicing is further illustrated by the increasing number of **human** diseases that have been attributed to mis-splicing events. Appropriate spatial and temporal generation of splicing variants demands that alternative splicing be subjected to extensive regulation, similar to transcriptional control. The Clk (Cdc2-like **kinase**) family has been implicated in splicing control and consists of at least four members. Through extensive screening of a chemical library, we found that a benzothiazole compound, TG003, had a potent inhibitory effect on the activity of Clk1/Sty. TG003 inhibited SF2/ASF-dependent splicing of beta-globin pre-mRNA in vitro by suppression of Clk-mediated phosphorylation. This drug also suppressed **serine/arginine-rich** protein phosphorylation, dissociation of nuclear speckles, and Clk1/Sty-dependent alternative splicing in mammalian cells. Consistently, administration of TG003 rescued the embryonic defects induced by excessive Clk activity in Xenopus. Thus, TG003, a novel inhibitor of Clk family will be a valuable tool to dissect the regulatory mechanisms involving **serine/arginine-rich** protein phosphorylation signaling pathways in vivo, and may be applicable for the therapeutic manipulation of abnormal splicing.

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ACCESSION NUMBER: 2003:583799 BIOSIS
DOCUMENT NUMBER: PREV200300573478

TITLE: MODULATION OF NUCLEAR SPECKLES AND SR PROTEINS IN INTESTINAL EPITHELIAL CELLS BY MEMBRANE-PERMEANT OXIDANTS.

AUTHOR(S): Zhu, Ya-Qin [Reprint Author]; Lu, Yu [Reprint Author]; Tan, Xiao-Di [Reprint Author]

CORPORATE SOURCE: Chicago, IL, USA

SOURCE: Digestive Disease Week Abstracts and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. T1040. e-file.
Meeting Info.: Digestive Disease 2003. FL, Orlando, USA. May 17-22, 2003. American Association for the Study of Liver Diseases; American Gastroenterological Association; American Society for Gastrointestinal Endoscopy; Society for Surgery of the Alimentary Tract.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 2003
Last Updated on STN: 10 Dec 2003

AB Background and Objective: Nuclear speckle is a nuclear subcompartment, which is associated with alternative splicing of pre-mRNA. It enriches a family of proteins, the SR (**serine/arginine-rich**) proteins, which play important roles in the splicing control. Recent investigations suggest that the alternative splicing process is altered during the GI inflammation. However, a large gap

exists in our understanding of how this process is modulated by inflammatory stimulation. Monochloramine (NH2Cl) is a membrane-permeant oxidant generated during inflammation in the GI tract. It stimulates fluid secretion and contributes to local tissue damage. However, the effect of NH2Cl on gene **expressions** in enterocytes is not clear. In the present study, we investigated whether NH2Cl induces structural changes of nuclear speckles and explored the mechanism through which NH2Cl modulates the architecture of nuclear speckles and phosphorylation of SR proteins in intestinal epithelial cells (IEC). Methods: IEC cells including HT-29 and Caco-2 lines were treated with NH2Cl. The distribution of nuclear speckles in IEC cells was determined by indirect immunofluorescence with an anti-SC35 monoclonal antibody. To identify phosphorylation status of SR proteins after NH2Cl treatment, we isolated total cellular protein from NH2Cl-stimulated IEC cells and performed western blot using mAb104. Results: Nuclear speckles recognized by anti-SC35 mAb were concentrated in distinct domains in resting IEC cells. Treatment of IEC cells with NH2Cl induced aggregation of nuclear speckles in IEC cells within 2 hrs. Furthermore, we found that NH2Cl up-regulates phosphorylation of SRp30 in IEC cells. This effect was in the dose-dependent manner. Pre-treatment of IEC cells with selective inhibitors of protein **kinase** C attenuated NH2Cl-induced aggregation of nuclear speckles and phosphorylation of SRp30. In addition, the PKC activity was elevated in NH2Cl-treated IEC cells. Phorbol 12-myristate-13-acetate, a classic PKC activator, mimics the NH2Cl effect on nuclear speckle distribution and SRp30 phosphorylation in IEC cells. Conclusions: The present study indicates that the dynamic distribution of nuclear speckles and phosphorylation of SR proteins in IEC cells are modulated by oxidants via distinctive signal pathways in IEC cells. This effect may participate in the inflammatory process of the gastrointestinal tract.

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ACCESSION NUMBER: 2003:212356 BIOSIS
DOCUMENT NUMBER: PREV200300212356
TITLE: An early ancestor in the evolution of splicing: A Trypanosoma cruzi **serine-arginine-rich** protein (TcSR) is functional in cis-splicing.
AUTHOR(S): Portal, Daniel; Espinosa, Joaquin M.; Lobo, Guillermo S.; Kadener, Sebastian; Pereira, Claudio A.; De La Mata, Manuel; Tang, Zhaohua; Lin, Ren-Jang; Kornblihtt, Alberto R.; Baralle, Francisco E.; Flawia, Mirtha M.; Torres, Hector N. [Reprint Author]
CORPORATE SOURCE: Facultad de Ciencias Exactas y Naturales, Instituto de Investigaciones en Ingenieria Genetica y Biologia Molecular, Consejo Nacional de Investigaciones Cientificas y Tecnicas, Universidad de Buenos Aires, Buenos Aires, Argentina
torres@proteus.dna.uba.ar
SOURCE: Molecular & Biochemical Parasitology, (March 2003) Vol. 127, No. 1, pp. 37-46. print.
CODEN: MBIPDP. ISSN: 0166-6851.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Apr 2003
Last Updated on STN: 30 Apr 2003

AB A novel **serine-arginine-rich** protein designated TcSR was identified in Trypanosoma cruzi. The deduced amino acid sequence reveals that TcSR is a member of the SR protein family of splicing factors that contains two RNA-binding domains at the N-terminal side and several **serine-arginine** repeats at the COOH-terminus. Over **expression** of either TcSR or the **human** SR-protein associated splicing factor/splicing factor 2

(ASF/SF2) in wild-type Schizosaccharomyces pombe, provoked an elongated phenotype similar to that of fission yeast over **expressing** the SR-containing splicing factor Prp2, a U2AF65 orthologue. When a double mutant strain lacking two SR protein-specific protein **kinases** was used, **expression** of TcSR or **human** SR ASF/SF2 splicing factor reverted the mutant to a wild-type phenotype. Transient **expression** of TcSR in HeLa cells stimulated the inclusion of the EDI exon of **human** fibronectin in an in vivo functional alternative cis-splicing assay. Inclusion was dependent on a splicing enhancer sequence present in the EDI exon. In addition, TcSR and peptides carrying TcSR-RS domain sequences were phosphorylated by a **human** SR protein **kinase**. These results indicate that TcSR is a member of the SR splicing network and that some components common to the trans- and cis-splicing machineries evolved from the early origins of the eukaryotic lineage.

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ACCESSION NUMBER: 2003:99385 BIOSIS
DOCUMENT NUMBER: PREV200300099385
TITLE: Exonic splicing enhancer-dependent selection of the bovine papillomavirus type 1 nucleotide 3225 3' splice site can be rescued in a cell lacking splicing factor ASF/SF2 through activation of the phosphatidylinositol 3-**kinase** /Akt pathway.
AUTHOR(S): Liu, Xuefeng; Mayeda, Akila; Tao, Mingfang; Zheng, Zhi-Ming [Reprint Author]
CORPORATE SOURCE: HIV and AIDS Malignancy Branch, Center for Cancer Research, NCI/NIH, 10 Center Dr., Rm. 10 S255, MSC-1868, Bethesda, MD, 20892-1868, USA
zhengt@exchange.nih.gov
SOURCE: Journal of Virology, (February 2003) Vol. 77, No. 3, pp. 2105-2115. print.
ISSN: 0022-538X (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Feb 2003
Last Updated on STN: 12 Feb 2003

AB Bovine papillomavirus type 1 (BPV-1) late pre-mRNAs are spliced in keratinocytes in a differentiation-specific manner: the late leader 5' splice site alternatively splices to a proximal 3' splice site (at nucleotide 3225) to **express** L2 or to a distal 3' splice site (at nucleotide 3605) to **express** L1. Two exonic splicing enhancers, each containing two ASF/SF2 (alternative splicing factor/splicing factor 2) binding sites, are located between the two 3' splice sites and have been identified as regulating alternative 3' splice site usage. The present report demonstrates for the first time that ASF/SF2 is required under physiological conditions for the **expression** of BPV-1 late RNAs and for selection of the proximal 3' splice site for BPV-1 RNA splicing in DT40-ASF cells, a genetically engineered chicken B-cell line that **expresses** only **human** ASF/SF2 controlled by a tetracycline-repressible promoter. Depletion of ASF/SF2 from the cells by tetracycline greatly decreased viral RNA **expression** and RNA splicing at the proximal 3' splice site while increasing use of the distal 3' splice site in the remaining viral RNAs. Activation of cells lacking ASF/SF2 through anti-immunoglobulin M-B-cell receptor cross-linking rescued viral RNA **expression** and splicing at the proximal 3' splice site and enhanced Akt phosphorylation and **expression** of the phosphorylated **serine/arginine-rich** (SR) proteins SRp30s (especially SC35) and SRp40. Treatment with wortmannin, a specific phosphatidylinositol 3-**kinase**/Akt **kinase** inhibitor, completely blocked the activation-induced activities. ASF/SF2 thus plays an important role in viral RNA **expression** and

splicing at the proximal 3' splice site, but activation-rescued viral RNA **expression** and splicing in ASF/SF2-depleted cells is mediated through the phosphatidylinositol 3-**kinase**/Akt pathway and is associated with the enhanced **expression** of other SR proteins.

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ACCESSION NUMBER: 2003:72130 BIOSIS
DOCUMENT NUMBER: PREV200300072130
TITLE: PSKH1, a novel splice factor compartment-associated serine **kinase**.
AUTHOR(S): Brede, Gaute; Solheim, Jorun; Prydz, Hans [Reprint Author]
CORPORATE SOURCE: Biotechnology Centre of Oslo, University of Oslo, Gaustadalleen 21, N-0349, Oslo, Norway hans.prydz@biotek.uio.no
SOURCE: Nucleic Acids Research, (December 1 2002) Vol. 30, No. 23, pp. 5301-5309. print.
ISSN: 0305-1048 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Jan 2003
Last Updated on STN: 29 Jan 2003

AB Small nuclear ribonucleoprotein particles (snRNPs) and non-snRNP splicing factors containing a **serine/arginine-rich** domain (SR proteins) concentrate in splicing factor compartments (SFCs) within the nucleus of interphase cells. Nuclear SFCs are considered mainly as storage sites for splicing factors, supplying splicing factors to active genes. The mechanisms controlling the interaction of the various spliceosome constituents, and the dynamic nature of the SFCs, are still poorly understood. We show here that endogenous PSKH1, a previously **cloned kinase**, is located in SFCs. Migration of PSKH1-FLAG into SFCs is enhanced during co-**expression** of T7-tagged ASF/SF2 as well as other members of the SR protein family, but not by two other non-SR nuclear proteins serving as controls. Similar to the SR protein **kinase** family, overexpression of PSKH1 led to reorganization of co-**expressed** T7-SC35 and T7-ASF/SF2 into a more diffuse nuclear pattern. This redistribution was not dependent on PSKH1 **kinase** activity. Different from the SR protein **kinases**, the SFC-associating features of PSKH1 were located within its catalytic **kinase** domain and within its C-terminus. Although no direct interaction was observed between PSKH1 and any of the SR proteins tested in pull-down or yeast two-hybrid assays, forced **expression** of PSKH1-FLAG was shown to stimulate distal splicing of an E1A minigene in HeLa cells. Moreover, a GST-ASF/SF2 fusion was not phosphorylated by PSKH1, suggesting an indirect mechanism of action on SR proteins. Our data suggest a mutual relationship between PSKH1 and SR proteins, as they are able to target PSKH1 into SFCs, while forced PSKH1 **expression** modulates nuclear dynamics and the function of co-**expressed** splicing factors.

L8 ANSWER 36 OF 78 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:523950 BIOSIS
DOCUMENT NUMBER: PREV200100523950
TITLE: SKY1 is involved in cisplatin-induced cell kill in Saccharomyces cerevisiae, and inactivation of its **human** homologue, SRPK1, induces cisplatin resistance in a **human** ovarian carcinoma cell line.
AUTHOR(S): Schenk, Paul W.; Boersma, Antonius W. M.; Brandsma, Jourica A.; den Dulk, Hans; Burger, Herman; Stoter, Gerrit; Brouwer, Jaap; Nooter, Kees [Reprint author]
CORPORATE SOURCE: Department of Medical Oncology, University Hospital

Rotterdam, Josephine Nefkens Building Room Be422, 3000 DR, Rotterdam, Netherlands
nooter@oncd.azr.nl

SOURCE: Cancer Research, (October 1, 2001) Vol. 61, No. 19, pp. 6982-6986. print.
CODEN: CNREA8. ISSN: 0008-5472.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Nov 2001
Last Updated on STN: 23 Feb 2002

AB The therapeutic potential of cisplatin, one of the most active and widely used anticancer drugs, is severely limited by the occurrence of cellular resistance. In this study, using budding yeast Saccharomyces cerevisiae as a model organism to identify novel drug resistance genes, we found that disruption of the yeast gene SKY1 (**serine/arginine-rich** protein-specific **kinase** from budding yeast) by either transposon insertion or one-step gene replacement conferred cellular resistance to cisplatin. Heterologous **expression** of the **human** SKY1 homologue SRPK1 (**serine/arginine-rich** protein-specific **kinase**) in SKY1 deletion mutant yeast cells restored cisplatin sensitivity, suggesting that SRPK1 is a cisplatin sensitivity gene, the inactivation of which could lead to cisplatin resistance. Subsequently, we investigated the role of SRPK1 in cisplatin sensitivity and resistance in **human** ovarian carcinoma A2780 cells using antisense oligodeoxynucleotides. Treatment of A2780 cells with antisense oligodeoxynucleotides directed against the translation initiation site of SRPK1 led to down-regulation of SRPK1 protein and conferred a 4-fold resistance to cisplatin. The **human** SRPK1 gene has not been associated with drug resistance before. Our new findings strongly suggest that SRPK1 is involved in cisplatin-induced cell kill and indicate that SRPK1 might potentially be of importance for studying clinical drug resistance.

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ACCESSION NUMBER: 2001:457350 BIOSIS
DOCUMENT NUMBER: PREV200100457350
TITLE: **Cloning** of **human** PRP4 reveals interaction with Clk1.
AUTHOR(S): Kojima, Tatsuya; Zama, Takeru; Wada, Kazuhiro; Onogi, Hiroshi; Hagiwara, Masatoshi [Reprint author]
CORPORATE SOURCE: Department of Functional Genomics, Medical Research Institute, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo, 113-8510, Japan
m.hagiwara.end@mri.tmd.ac.jp
SOURCE: Journal of Biological Chemistry, (August 24, 2001) Vol. 276, No. 34, pp. 32247-32256. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Sep 2001
Last Updated on STN: 22 Feb 2002

AB Prp4 is a protein **kinase** of Schizosaccharomyces pombe identified through its role in pre-mRNA splicing, and belongs to a **kinase** family including mammalian **serine/arginine-rich** protein-specific **kinases** and Clks, whose substrates are **serine/arginine-rich** proteins. We **cloned human** PRP4 (hPRP4) full-length cDNA and the antiserum raised against a partial peptide of hPRP4 recognized 170-kDa polypeptide in HeLa S3 cell extracts. Northern blot analysis revealed that hPRP4 mRNA was ubiquitously **expressed** in multiple tissues. The extended NH2-terminal region of hPRP4 contains an arginine/serine-rich domain and putative nuclear localization signals. hPRP4 phosphorylated and

interacted with SF2/ASF, one of the essential splicing factors. Indirect immunofluorescence analysis revealed that endogenous hPRP4 was distributed in a nuclear speckled pattern and colocalized with SF2/ASF in HeLa S3 cells. Furthermore, hPRP4 interacted directly with Clk1 on its COOH terminus, and the arginine/serine-rich domain of hPRP4 was phosphorylated by Clk1 in vitro. Overexpression of Clk1 caused redistribution of hPRP4, from the speckled to the diffuse pattern in nucleoplasm, whereas inactive mutant of Clk1 caused no change of hPRP4 localization. These findings suggest that the NH2-terminal region of hPRP4 may play regulatory roles under an unidentified signal transduction pathway through Clk1.

L8 ANSWER 38 OF 78 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1999:241635 BIOSIS
DOCUMENT NUMBER: PREV199900241635
TITLE: The subcellular localization of SF2/ASF is regulated by direct interaction with SR protein **kinases** (SRPKs).
AUTHOR(S): Koizumi, Jun; Okamoto, Yoshichika; Onogi, Hiroshi; Mayeda, Akila; Krainer, Adrian R.; Hagiwara, Masatoshi [Reprint author]
CORPORATE SOURCE: Department of Functional Genomics, Medical Research Institute, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo, 113, Japan
SOURCE: Journal of Biological Chemistry, (April 16, 1999) Vol. 274, No. 16, pp. 11125-11131. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Jun 1999
Last Updated on STN: 17 Jun 1999

AB **Serine/arginine-rich** (SR) proteins play an important role in constitutive and alternative pre-mRNA splicing. The C-terminal arginine-serine domain of these proteins, such as SF2/ASF, mediates protein-protein interactions and is phosphorylated in vivo. Using glutathione S-transferase (GST)-SF2/ASF-affinity chromatography,the SF2/ASF **kinase** activity was co-purified from HeLa cells witha 95-kDa protein, which was recognized by an anti-SR protein **kinase** (SRPK) 1 monoclonal antibody. **Recombinant** SRPK1 and SRPK2 bound to and phosphorylated GST-SF2/ASF in vitro. Phosphopeptide mapping showed that identical sites were phosphorylated in the pull-down **kinase** reaction with HeLa extracts and by **recombinant** SRPKs. Epitope-tagged SF2/ASF transiently **expressed** in COS7 cells co-immunoprecipitated with SRPKs. Deletion analysis mapped thephosphorylation sites to a region containing an (Arg-Ser)8 repeat beginning at residue 204, and far-Western analysis showed that the region is required for binding of SRPKs to SF2/ASF.Further binding studies showed that SRPKs bound unphosphorylatedSF2/ASF but did not bind phosphorylated SF2/ASF. **Expression** of an SRPK2 **kinase**-inactive mutant caused accumulation of SF2/ASF in the cytoplasm. These results suggest that the formation of complexes between SF2/ASF and SRPKs, which is influenced by the phosphorylation state of SF2/ASF, may have regulatory roles in the assembly and localization of this splicing factor.

L8 ANSWER 39 OF 78 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1997:495482 BIOSIS
DOCUMENT NUMBER: PREV199799794685
TITLE: In vivo regulation of alternative pre-mRNA splicing by the Clk1 protein **kinase**.
AUTHOR(S): Duncan, Peter I.; Stojdl, David F.; Marius, Ricardo M.; Bell, John C. [Reprint author]
CORPORATE SOURCE: Ottawa Regional Cancer Centre, 501 Smyth Rd., Ottawa, ON

K1H 8L6, Canada
SOURCE: Molecular and Cellular Biology, (1997) Vol. 17, No. 10, pp. 5996-6001.
CODEN: MCEBD4. ISSN: 0270-7306.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Nov 1997
Last Updated on STN: 10 Dec 1997

AB Controlled **expression** of cellular and viral genes through alternative precursor messenger RNA (pre-mRNA) splicing requires **serine/arginine-rich** (SR) proteins. The Clk1 **kinase**, which phosphorylates SR proteins, is regulated through alternative splicing of the Clk1 pre-mRNA, yielding mRNAs encoding catalytically active and truncated inactive polypeptides (Clk1 and Clk1-T, respectively). We present evidence that Clk1 and Clk1-T proteins regulate the splicing of Clk1 and adenovirus pre-mRNAs in vivo. The peptide domain encoded by the alternatively spliced exon of Clk1 is essential for the regulatory activity of the Clk1 **kinase**. This is the first direct demonstration of an in vivo link between alternative splicing and protein **kinase** activity.

L8 ANSWER 40 OF 78 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:453732 BIOSIS
DOCUMENT NUMBER: PREV199598468032
TITLE: Identification of a plant **serine-arginine -rich** protein similar to the mammalian splicing factor SF2/ASF.
AUTHOR(S): Lazar, Gabor; Schaal, Thomas; Maniatis, Tom; Goodman, Howard M. [Reprint author]
CORPORATE SOURCE: Dep. Mol. Biol., Massachusetts General Hosp., Wellman Building 11, 50 Blossom St., Boston, MA 02114, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1995) Vol. 92, No. 17, pp. 7672-7676.
CODEN: PNASA6. ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
OTHER SOURCE: Genbank-M98340
ENTRY DATE: Entered STN: 27 Oct 1995
Last Updated on STN: 14 Dec 1995

AB We show that the higher plant Arabidopsis thaliana has a **serine-arginine-rich** (SR) protein family whose members contain a phosphoepitope shared by the animal SR family of splicing factors. In addition, we report the **cloning** and characterization of a cDNA encoding a higher-plant SR protein from Arabidopsis, SR1, which has striking sequence and structural homology to the **human** splicing factor SF2/ASF. Similar to SF2/ASF, the plant SR1 protein promotes splice site switching in mammalian nuclear extracts. A novel feature of the Arabidopsis SR protein is a C-terminal domain containing a high concentration of proline, serine, and lysine residues (PSK domain), a composition reminiscent of histones. This domain includes a putative phosphorylation site for the mitotic **kinase** cyclin/p34-cdc2.

L8 ANSWER 41 OF 78 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1994:343600 BIOSIS
DOCUMENT NUMBER: PREV199497356600
TITLE: A serine **kinase** regulates intracellular localization of splicing factors in the cell cycle.
AUTHOR(S): Gui, Jian-Fang; Lane, William S.; Fu, Xiang-Dong [Reprint author]
CORPORATE SOURCE: Div. Cell. Mol. Med., Univ. Calif. San Diego, 9500 Gilman

Dr., La Jolla, CA 92093-0651, USA
SOURCE: Nature (London), (1994) Vol. 369, No. 6482, pp. 678-683.
CODEN: NATUAS. ISSN: 0028-0836.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Aug 1994
Last Updated on STN: 8 Aug 1994

AB Small nuclear ribonucleoprotein particles (snRNPs) and non-snRNP splicing factors containing a **serine/arginine-rich** domain (SR proteins) concentrate in 'speckles' in the nucleus of interphase cells. It is believed that nuclear speckles act as storage sites for splicing factors while splicing occurs on nascent transcripts. Splicing factors redistribute in response to transcription inhibition or viral infection, and nuclear speckles break down and reform as cells progress through mitosis. We have now identified and **cloned** a **kinase**, SRPK1, which is regulated by the cell cycle and is specific for SR proteins; this **kinase** is related to a Caenorhahditis elegans **kinase** and to the fission yeast **kinase** Dsk1 (reference 7). SRPK1 specifically induces the disassembly of nuclear speckles, and a high level of SRPK1 inhibits splicing in vitro. Our results indicate that SRPK1 may have a central role in the regulatory network for splicing, controlling the intranuclear distribution of splicing factors in interphase cells, and the reorganization of nuclear speckles during mitosis.

L8 ANSWER 42 OF 78 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:519021 SCISEARCH
THE GENUINE ARTICLE: 824RA
TITLE: Manipulation of alternative splicing by a newly developed inhibitor of Clks
AUTHOR: Muraki M; Ohkawara B; Hosoya T; Onogi H; Koizumi J; Koizumi T; Sumi K; Jun-ichiro Y; Murray M V; Kimura H; Furuichi K; Shibuya H; Krainer A R; Suzuki M; Hagiwara M (Reprint)
CORPORATE SOURCE: Tokyo Med & Dent Univ, Sch Biomed Sci, Gene Express Lab, Bunkyo Ku, 1-5-45 Yushima, Tokyo 1138510, Japan (Reprint); Tokyo Med & Dent Univ, Sch Biomed Sci, Gene Express Lab, Bunkyo Ku, Tokyo 1138510, Japan; Tokyo Med & Dent Univ, Med Res Inst, Dept Funct Genom, Tokyo, Japan; Tokyo Med & Dent Univ, Med Res Inst, Dept Mol & Cellular Biol, Tokyo, Japan; Gifu Univ, Grad Sch Med, Div Regenerat & Adv Med Sci, Gifu 5011193, Japan; Yamanouchi Pharmaceut Co Ltd, Mol Med Labs, Tsukuba, Ibaraki 3058585, Japan; Cold Spring Harbor Lab, Cold Spring Harbor, NY 11724 USA; Kyoto Univ, Grad Sch Med, Horizontal Med Res Org, Nucl Funct & Dynam Unit, Kyoto 6068501, Japan
COUNTRY OF AUTHOR: Japan; USA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (4 JUN 2004) Vol. 279, No. 23, pp. 24246-24254.
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3996 USA.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 59
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The regulation of splice site usage provides a versatile mechanism for controlling gene **expression** and for the generation of proteome diversity, playing an essential role in many biological processes. The importance of alternative splicing is further illustrated by the increasing number of **human** diseases that have been attributed to mis-splicing events. Appropriate spatial and temporal generation of

splicing variants demands that alternative splicing be subjected to extensive regulation, similar to transcriptional control. The Clk (Cdc2-like **kinase**) family has been implicated in splicing control and consists of at least four members. Through extensive screening of a chemical library, we found that a benzothiazole compound, TG003, had a potent inhibitory effect on the activity of Clk1/Sty. TG003 inhibited SF2/ASF-dependent splicing of beta-globin pre-mRNA in vitro by suppression of Clk-mediated phosphorylation. This drug also suppressed **serine /arginine-rich** protein phosphorylation, dissociation of nuclear speckles, and Clk1/Sty-dependent alternative splicing in mammalian cells. Consistently, administration of TG003 rescued the embryonic defects induced by excessive Clk activity in Xenopus. Thus, TG003, a novel inhibitor of Clk family will be a valuable tool to dissect the regulatory mechanisms involving **serine/arginine-rich** protein phosphorylation signaling pathways in vivo, and may be applicable for the therapeutic manipulation of abnormal splicing.

L8 ANSWER 43 OF 78 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:283495 SCISEARCH
THE GENUINE ARTICLE: 658TB
TITLE: An early ancestor in the evolution of splicing: a Trypanosoma cruzi **serine-arginine-rich** protein (TcSR) is functional in cis-splicing
AUTHOR: Portal D; Espinosa J M; Lobo G S; Kadener S; Pereira C A; De la Mata M; Tang Z H; Lin R J; Kornblihtt A R; Baralle F E; Flawia M M; Torres H N (Reprint)
CORPORATE SOURCE: Univ Buenos Aires, Fac Ciencias Exactas & Nat, Inst Invest Ingn Genet & Biol Mol, Consejo Nacl Invest Cient & Tecn, Buenos Aires, DF, Argentina (Reprint); Univ Buenos Aires, Fac Ciencias Exactas & Nat, Lab Fisiol & Biol Mol, Buenos Aires, DF, Argentina; Beckman Res Inst City Hope, Dept Mol Biol, Duarte, CA USA; Int Ctr Genet Engn & Biotechnol, I-34012 Trieste, Italy
COUNTRY OF AUTHOR: Argentina; USA; Italy
SOURCE: MOLECULAR AND BIOCHEMICAL PARASITOLOGY, (MAR 2003) Vol. 127, No. 1, pp. 37-46.
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
ISSN: 0166-6851.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 58

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A novel **serine-arginine-rich** protein designated TcSR was identified in Trypanosoma cruzi. The deduced amino acid sequence reveals that TcSR is a member of the SR protein family of splicing factors that contains two RNA-binding domains at the N-terminal side and several **serine-arginine** repeats at the COOH-terminus. Over **expression** of either TcSR or the **human** SR-protein associated splicing factor/splicing factor 2 (ASF/SF2) in wild-type Schizosaccharomyces pombe, provoked an elongated phenotype similar to that of fission yeast over **expressing** the SR-containing splicing factor Prp2, a U2AF(65) orthologue. When a double mutant strain lacking two SR protein-specific protein **kinases** was used, **expression** of TcSR or **human** SR ASF/SF2 splicing factor reverted the mutant to a wild-type phenotype. Transient **expression** of TcSR in HeLa cells stimulated the inclusion of the EDI exon of **human** fibronectin in an in vivo functional alternative cis-splicing assay. Inclusion was dependent on a splicing enhancer sequence present in the EDI exon. In addition, TcSR and peptides carrying TcSR-RS domain sequences were phosphorylated by a **human** SR protein **kinase**. These results indicate that TcSR is a member

of the SR splicing network and that some components common to the trans- and cis-splicing machineries evolved from the early origins of the eukaryotic lineage. (C) 2002 Elsevier Science B.V. All rights reserved.

L8 ANSWER 44 OF 78 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:102181 SCISEARCH
THE GENUINE ARTICLE: 637AD
TITLE: Exonic splicing enhancer-dependent selection of the bovine papillornavirus type 1 nucleotide 3225 3 ' splice site can be rescued in a cell lacking splicing factor ASF/SF2 through activation of the phosphatidylinositol 3-**kinase**/Akt pathway
AUTHOR: Liu X F; Mayeda A; Tao M F; Zheng Z M (Reprint)
CORPORATE SOURCE: NCI, HIV & AIDS Malignancy Branch, Ctr Canc Res, NIH, Rm 10 S255, 10 Ctr Dr, MSC-1868, Bethesda, MD 20892 USA (Reprint); NCI, HIV & AIDS Malignancy Branch, Ctr Canc Res, NIH, Bethesda, MD 20892 USA; Univ Miami, Sch Med, Dept Biochem & Mol Biol, Miami, FL 33136 USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF VIROLOGY, (FEB 2003) Vol. 77, No. 3, pp. 2105-2115.
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
ISSN: 0022-538X.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 60

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Bovine papillomavirus type 1 (BPV-1) late pre-mRNAs are spliced in keratinocytes in a differentiation-specific manner: the late leader 5' splice site alternatively splices to a proximal 3' splice site (at nucleotide 3225) to **express** L2 or to a distal 3' splice site (at nucleotide 3605) to **express** L1. Two exonic splicing enhancers, each containing two ASF/SF2 (alternative splicing factor/splicing factor 2) binding sites, are located between the two 3' splice sites and have been identified as regulating alternative 3' splice site usage. The present report demonstrates for the first time that ASF/SF2 is required under physiological conditions for the **expression** of BPV-1 late RNAs and for selection of the proximal 3' splice site for BPV-1 RNA splicing in DT40-ASF cells, a genetically engineered chicken B-cell line that **expresses** only **human** ASF/SF2 controlled by a tetracycline-repressible promoter. Depletion of ASF/SF2 from the cells by tetracycline greatly decreased viral RNA **expression** and RNA splicing at the proximal 3' splice site while increasing use of the distal 3' splice site in the remaining viral RNAs. Activation of cells lacking ASF/SF2 through anti-immunoglobulin M-B-cell receptor cross-linking rescued viral RNA **expression** and splicing at the proximal 3' splice site and enhanced Akt phosphorylation and **expression** of the phosphorylated **serine/arginine-rich** (SR) proteins SRp30s (especially SC35) and SRp40. Treatment with wortmannin, a specific phosphatidylinositol 3-**kinase**/Akt **kinase** inhibitor, completely blocked the activation-induced activities. ASF/SF2 thus plays an important role in viral RNA **expression** and splicing at the proximal 3' splice site, but activation-rescued viral RNA **expression** and splicing in ASF/SF2-depleted cells is mediated through the phosphatidylinositol 3-**kinase**/Akt pathway and is associated with the enhanced **expression** of other SR proteins.

L8 ANSWER 45 OF 78 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:800566 SCISEARCH
THE GENUINE ARTICLE: 479PB

TITLE: SKY1 is involved in cisplatin-induced cell kill in Saccharomyces cerevisiae, and inactivation of its **human** homologue, SRPK1, induces cisplatin resistance in a **human** ovarian carcinoma cell line

AUTHOR: Schenk P W; Boersma A W M; Brandsma J A; den Dulk H; Burger H; Stoter G; Brouwer J; Nooter K (Reprint)

CORPORATE SOURCE: Univ Rotterdam Hosp, Dept Med Oncol, Dr Daniel Den Hoed Canc Ctr, Josephine Nefkens Bldg Room Be422, POB 1738, NL-3000 DR Rotterdam, Netherlands (Reprint); Univ Rotterdam Hosp, Dept Med Oncol, Dr Daniel Den Hoed Canc Ctr, NL-3000 DR Rotterdam, Netherlands; Leiden Univ, Gorlaeus Labs, Leiden Inst Chem, Dept Mol Genet, NL-2300 RA Leiden, Netherlands

COUNTRY OF AUTHOR: Netherlands

SOURCE: CANCER RESEARCH, (1 OCT 2001) Vol. 61, No. 19, pp. 6982-6986.
Publisher: AMER ASSOC CANCER RESEARCH, PO BOX 11806, BIRMINGHAM, AL 35202 USA.
ISSN: 0008-5472.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 23

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The therapeutic potential of cisplatin, one of the most active and widely used anticancer drugs, is severely limited by the occurrence of cellular resistance. In this study, using budding yeast Saccharomyces cerevisiae as a model organism to identify novel drug resistance genes, we found that disruption of the yeast gene SKY1 (**serine/arginine-rich** protein-specific **kinase** from budding yeast) by either transposon insertion or one-step gene replacement conferred cellular resistance to cisplatin. Heterologous **expression** of the **human** SKY1 homologue SRPK1 (**serine/arginine-rich** protein-specific **kinase**) in SkY1 deletion mutant yeast cells restored cisplatin sensitivity, suggesting that SRPK1 is a cisplatin sensitivity gene, the inactivation of which could lead to cisplatin resistance. Subsequently, we investigated the rote of SRPK1 in cisplatin sensitivity and resistance in **human** ovarian carcinoma A2780 cells using antisense oligodeoxynucleotides. Treatment of A2780 cells with antisense oligodeoxynucleotides directed against the translation initiation site of SRPK1 led to downregulation of SRPK1 protein and conferred a 4-fold resistance to cisplatin. The **human** SRPK1 gene has not been associated with drug resistance before. Our new findings strongly suggest that SRPK1 is involved in cisplatin-induced cell kill and indicate that SRPK1 might potentially be of importance for studying clinical drug resistance.

L8 ANSWER 46 OF 78 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:687406 SCISEARCH

THE GENUINE ARTICLE: 465WT

TITLE: **Cloning** of **human** PRP4 reveals interaction with Clk1

AUTHOR: Kojima T; Zama T; Wada K; Onogi H; Hagiwara M (Reprint)

CORPORATE SOURCE: Tokyo Med & Dent Univ, Med Res Inst, Dept Funct Genom, Bunkyo Ku, 1-5-45 Yushima, Tokyo 1138510, Japan (Reprint); Tokyo Med & Dent Univ, Med Res Inst, Dept Funct Genom, Bunkyo Ku, Tokyo 1138510, Japan; Keio Univ, Sch Med, Dept Med, Shinjuku Ku, Tokyo 1600016, Japan; Tokai Univ, Sch Med, Inst Med Sci, Isehara, Kanagawa 2591193, Japan; Tokai Univ, Sch Med, Dept Med, Isehara, Kanagawa 2591193, Japan

COUNTRY OF AUTHOR: Japan

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (24 AUG 2001) Vol. 276, No. 34, pp. 32247-32256.
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 48

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Prp4 is a protein **kinase** of Schizosaccharomyces pombe identified through its role in pre-mRNA splicing, and belongs to a **kinase** family including mammalian **serine/arginine-rich** protein-specific **kinases** and Clks, whose substrates are **serine/arginine-rich** proteins. We **cloned human** PRP4 (hPRP4) full-length cDNA and the antiserum raised against a partial peptide of hPRP4 recognized 170-kDa polypeptide in HeLa S3 cell extracts. Northern blot analysis revealed that hPRP4 mRNA was ubiquitously **expressed** in multiple tissues. The extended NH2-terminal region of hPRP4 contains an arginine/serine-rich domain and putative nuclear localization signals. hPRP4 phosphorylated and interacted with SF2/ASF, one of the essential splicing factors. Indirect immunofluorescence analysis revealed that endogenous hPRP4 was distributed in a nuclear speckled pattern and colocalized with SF2/ASF in HeLa S3 cells. Furthermore, hPRP4 interacted directly with Clk1 on its COOH terminus, and the arginine/serine-rich domain of hPRP4 was phosphorylated by Clk1 in vitro. Overexpression of Clk1 caused redistribution of hPRP4, from the speckled to the diffuse pattern in nucleoplasm, whereas inactive mutant of Clk1 caused no change of hPRP4 localization. These findings suggest that the NH2-terminal region of hPRP4 may play regulatory roles under an unidentified signal transduction pathway through Clk1.

L8 ANSWER 47 OF 78 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:227333 SCISEARCH
THE GENUINE ARTICLE: 294LT
TITLE: A **human** importin-beta family protein, transportin-SR2, interacts with the phosphorylated RS domain of SR proteins
AUTHOR: Lai M C; Lin R I; Huang S Y; Tsai C W; Tarn W Y (Reprint)
CORPORATE SOURCE: ACAD SINICA, INST BIOMED SCI, 128 ACAD RD, SECT 2, TAIPEI 11529, TAIWAN (Reprint); ACAD SINICA, INST BIOMED SCI, TAIPEI 11529, TAIWAN
COUNTRY OF AUTHOR: TAIWAN
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (17 MAR 2000) Vol. 275, No. 11, pp. 7950-7957.
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 45

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Serine/arginine-rich** proteins (SR proteins) are mainly involved in the splicing of precursor mRNA. RS domains are also found in proteins that have influence on other aspects of gene **expression**. Proteins that contain an RS domain are often located in the speckled domains of the nucleus. Here we show that the RS domain derived from a **human** papillomavirus E2 transcriptional activator can target a heterologous protein to the nucleus, as it does in many other SR proteins, hut insufficient for localization in speckles. By using E2 as a bait in a yeast two-hybrid screen, we identified a

human importin-beta family protein that is homologous to yeast Mtr10p and almost identical to **human** transportin-SR. This transportin-SR2 (TRN-SR2) protein can interact with several cellular SR proteins. More importantly, we demonstrated that TRN-SR2 can directly interact with phosphorylated, but not unphosphorylated, RS domains. Finally, an indirect immunofluoresence study revealed that a transiently **expressed** TRN-SR2 mutant lacking the N-terminal region becomes localized to the nucleus in a speckled pattern that coincides with the distribution of the SR protein SC35, Thus, our results likely reflect a role of TRN-SR2 in the cellular trafficking of phosphorylated SR proteins.

L8 ANSWER 48 OF 78 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 95:554016 SCISEARCH
THE GENUINE ARTICLE: RP748
TITLE: IDENTIFICATION OF A PLANT **SERINE-ARGININE-RICH** PROTEIN SIMILAR TO THE MAMMALIAN SPLICING FACTOR SF2/ASF
AUTHOR: LAZAR G; SCHAAL T; MANIATIS T; GOODMAN H M (Reprint)
CORPORATE SOURCE: MASSACHUSETTS GEN HOSP, DEPT BIOL MOLEC, WELLMAN BLDG 11, 50 BLOSSOM ST, BOSTON, MA, 02114 (Reprint); MASSACHUSETTS GEN HOSP, DEPT BIOL MOLEC, BOSTON, MA, 02114; HARVARD UNIV, SCH MED, DEPT GENET, BOSTON, MA, 02115; HARVARD UNIV, DEPT MOLEC & CELLULAR BIOL, CAMBRIDGE, MA, 02138
COUNTRY OF AUTHOR: USA
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (15 AUG 1995) Vol. 92, No. 17, pp. 7672-7676.
ISSN: 0027-8424.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 45

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We show that the higher plant Arabidopsis thaliana has a **serine-arginine-rich** (SR) protein family whose members contain a phosphoepitope shared by the animal SR family of splicing factors, In addition, we report the **cloning** and characterization of a cDNA encoding a higher-plant SR protein from Arabidopsis, SR1, which has striking sequence and structural homology to the **human** splicing factor SF2/ASF, Similar to SF2/ASF, the plant SR1 protein promotes splice site switching in mammalian nuclear extracts, A novel feature of the Arabidopsis SR protein is a C-terminal domain containing a high concentration of proline, serine, and lysine residues (PSK domain), a composition reminiscent of histones, This domain includes a putative phosphorylation site for the mitotic **kinase** cyclin/p34(cdc2).

L8 ANSWER 49 OF 78 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:248644 HCAPLUS
DOCUMENT NUMBER: 142:274057
TITLE: Sequences of **human** schizophrenia related genes and use for diagnosis, prognosis and therapy
INVENTOR(S): Liew, Choong-chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 41
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2004241727	A1	20041202	US 2004-812731	20040330
US 2004014059	A1	20040122	US 2002-268730	20021009
US 2004241727	A1	20041202	US 2004-812731	20040330
US 2004248169	A1	20041209	US 2004-812737	20040330
WO 2004112589	A2	20041229	WO 2004-US20836	20040621

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:	US 1999-115125P	P	19990106
	US 2000-477148	B1	20000104
	US 2002-268730	A2	20021009
	US 2003-601518	A2	20030620
	US 2004-802875	A2	20040312
	US 2004-812731	A	20040330
	US 2001-271955P	P	20010228
	US 2001-275017P	P	20010312
	US 2001-305340P	P	20010713
	US 2002-85783	A2	20020228
	US 2004-809675	A	20040325

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing and monitoring diseases using gene-specific and/or tissue-specific primers. The present invention also describes methods by which delineation of the sequence and/or quantitation of the **expression** levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L8 ANSWER 50 OF 78 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2005:248643 HCAPLUS
DOCUMENT NUMBER:	142:274056
TITLE:	Sequences of **human** schizophrenia related genes and use for diagnosis, prognosis and therapy
INVENTOR(S):	Liew, Choong-Chin
PATENT ASSIGNEE(S):	Chondrogene Limited, Can.
SOURCE:	U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	41

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004241727	A1	20041202	US 2004-812731	20040330
US 2004014059	A1	20040122	US 2002-268730	20021009
US 2004241727	A1	20041202	US 2004-812731	20040330
US 2004248169	A1	20041209	US 2004-812737	20040330
WO 2004112589	A2	20041229	WO 2004-US20836	20040621

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 1999-115125P	P	19990106
US 2000-477148	B1	20000104
US 2002-268730	A2	20021009
US 2003-601518	A2	20030620
US 2004-802875	A2	20040312
US 2004-812731	A	20040330
US 2001-271955P	P	20010228
US 2001-275017P	P	20010312
US 2001-305340P	P	20010713
US 2002-85783	A2	20020228
US 2004-809675	A	20040325

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing and monitoring diseases using gene-specific and/or tissue-specific primers. The present invention also describes methods by which delineation of the sequence and/or quantitation of the **expression** levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L8 ANSWER 51 OF 78 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:112850 HCAPLUS
DOCUMENT NUMBER: 142:153469
TITLE: Gene **expression** profiles and biomarkers for the detection of lung disease-related and other disease-related gene transcripts in blood
INVENTOR(S): Liew, Choong-chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 155 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 41
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004241728	A1	20041202	US 2004-812764	20040330
US 2004014059	A1	20040122	US 2002-268730	20021009
US 2004241728	A1	20041202	US 2004-812764	20040330
US 2004248169	A1	20041209	US 2004-812737	20040330
WO 2004112589	A2	20041229	WO 2004-US20836	20040621

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 1999-115125P	P	19990106
US 2000-477148	B1	20000104
US 2002-268730	A2	20021009
US 2003-601518	A2	20030620
US 2004-802875	A2	20040312
US 2004-812764	A	20040330
US 2001-271955P	P	20010228
US 2001-275017P	P	20010312
US 2001-305340P	P	20010713
US 2002-85783	A2	20020228
US 2004-809675	A	20040325

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing and monitoring diseases using gene-specific and/or tissue-specific primers. Affymetrix **Human** Genome U133 and ChondroChip microarrays were used to detect differentially **expressed** gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention also describes methods by which delineation of the sequence and/or quantitation of the **expression** levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L8 ANSWER 52 OF 78 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:112848 HCAPLUS
DOCUMENT NUMBER: 142:153468
TITLE: Gene **expression** profiles and biomarkers for the detection of lung disease-related and other disease-related gene transcripts in blood
INVENTOR(S): Liew, Choong-chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 155 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 41
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004241728	A1	20041202	US 2004-812764	20040330
US 2004014059	A1	20040122	US 2002-268730	20021009
US 2004241728	A1	20041202	US 2004-812764	20040330
US 2004248169	A1	20041209	US 2004-812737	20040330
WO 2004112589	A2	20041229	WO 2004-US20836	20040621

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,

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            AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
            EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
            SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
            SN, TD, TG
PRIORITY APPLN. INFO.:                      US 1999-115125P     P  19990106
                                            US 2000-477148      B1 20000104
                                            US 2002-268730      A2 20021009
                                            US 2003-601518      A2 20030620
                                            US 2004-802875      A2 20040312
                                            US 2004-812764      A  20040330
                                            US 2001-271955P     P  20010228
                                            US 2001-275017P     P  20010312
                                            US 2001-305340P     P  20010713
                                            US 2002-85783       A2 20020228
                                            US 2004-809675      A  20040325
COMMAND INTERRUPTED

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Desk by telephone or via SEND in the STNMAIL file.

=> e boyds j/ay
'BOYDS J' IS NOT A VALID NUMERIC VALUE
'AY' IS NOT A VALID EXPAND FIELD CODE FOR FILE 'BIOSIS'
'AY' IS NOT A VALID EXPAND FIELD CODE FOR FILE 'EMBASE'
'AY' IS NOT A VALID EXPAND FIELD CODE FOR FILE 'MEDLINE'
'AY' IS NOT A VALID EXPAND FIELD CODE FOR FILE 'SCISEARCH'
'AY' IS NOT A VALID EXPAND FIELD CODE FOR FILE 'LIFESCI'
'BOYDS J' IS NOT A VALID NUMERIC VALUE
'BOYDS J' IS NOT A VALID NUMERIC VALUE
Only valid numeric terms can be EXPANDed in numeric fields.  Valid
numeric terms are zero and any term with an absolute value between 1
E-78 and 1 E74.  Non-numeric characters are not permitted in the
EXPAND command for numeric fields.  To see a list of numeric and text
fields in the current file, enter "HELP SFIELDS" at an arrow
prompt (=>).

=> e boyds j y/au
E1            1     BOYDS G/AU
E2            1     BOYDS J A/AU
E3            0 --> BOYDS J Y/AU
E4            1     BOYDS L/AU
E5            1     BOYDSS ANDREW W/AU
E6           17     BOYDSTON A J/AU
E7            6     BOYDSTON ANDREW J/AU
E8            3     BOYDSTON C M/AU
E9            1     BOYDSTON CH M/AU
E10           1     BOYDSTON CHRISTY M/AU
E11           1     BOYDSTON D/AU
E12           1     BOYDSTON D N/AU

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E1            2     YE IN HAE/AU
E2            1     YE INN SUK/AU
E3         1892 --> YE J/AU
E4           13     YE J A/AU
E5          243     YE J B/AU
E6           42     YE J C/AU
E7           32     YE J D/AU
E8           20     YE J F/AU
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E11         137      YE J J/AU
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E3         1117 --> YAN C/AU
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E5          124      YAN C C/AU
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E7            3      YAN C CHAN/AU
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E11          54      YAN C G/AU
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E3          234 --> KETCHUM K A/AU
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E7          188      KETCHUM KAREN A/AU
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E9            2      KETCHUM KATHY/AU
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E11           4      KETCHUM KEVIN/AU
E12           3      KETCHUM KEVIN L/AU

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                "KETCHUM KAREN"/AU OR "KETCHUM KAREN A"/AU OR "KETCHUM KAREN
                ANN"/AU)

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E3          100 --> DIFRANCESCO V/AU
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E6            1      DIFRANCESO D/AU
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E9            1      DIFRANCESO ROBIN/AU
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E12           1     BEASLEY EDWARD EVANS/AU

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L3           326 S L1 AND L2
L4       7000132 S CLON? OR EXPRESS? OR RECOMBINANT
L5           207 S L3 AND L4
L6           116 S HUMAN AND L5
L7           696 S "SERINE ARGININE RICH"
L8            78 S L6 AND L7
                 E BOYDS J Y/AU
                 E YE J/AU
L9          1892 S E3
                 E YAN C/AU
L10         1117 S E3
                 E KETCHUM K A/AU
L11          480 S E3-E8
                 E DIFRANCESCO V/AU
L12          117 S E3-E4
                 E BEASLEY E M/AU
L13        31699 S E3\
L14          324 S E3

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L15         3624 L9 OR L10 OR L11 OR L12 OR L14

=> s l2 and l15
L16             1 L2 AND L15

=> d all
AB   The present invention is directed to detection and measurement of gene
     transcripts and their equivalent nucleic acid products in blood.
Specifically
     provided is anal. performed on a drop of blood for detecting, diagnosing
     and monitoring diseases using gene-specific and/or tissue-specific
     primers.  Affymetrix Human Genome U133 and ChondroChip
     microarrays were used to detect differentially expressed gene
     transcripts in hypertension, obesity, allergy, systemic steroids, coronary
```

artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention also describes methods by which delineation of the sequence and/or quantitation of the **expression** levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 recordsfor this document necessitated by thelarge number of index entries required tofully index the document and publicationsystem constraints.].

L16 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:157957 HCAPLUS
DN 136:195349
ED Entered STN: 01 Mar 2002
TI Protein, gene and cDNA sequences of human protein kinase sequence homolog and diagnostic and therapeutic uses thereof
IN Yan, Chunhua; Ye, Jane; **Ketchum, Karen A.**; Di Francesco, Valentina; Beasley, Ellen M.
PA Applera Corporation, USA
SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N009-00
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 1, 7, 13
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002016567	A2	20020228	WO 2001-US26389	20010824
	WO 2002016567	A3	20030130		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2002076783	A1	20020620	US 2001-810671	20010319
	US 6455291	B2	20020924		
	CA 2421062	AA	20020228	CA 2001-2421062	20010824
	AU 2001086687	A5	20020304	AU 2001-86687	20010824
	EP 1313844	A2	20030528	EP 2001-966150	20010824
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	JP 2004522413	T2	20040729	JP 2002-522241	20010824
	US 2002119548	A1	20020829	US 2002-109854	20020401
	US 6630337	B2	20031007		
	US 2003134319	A1	20030717	US 2003-339656	20030110
	US 6733978	B2	20040511		
	US 2004152123	A1	20040805	US 2004-801671	20040317
PRAI	US 2000-227470P	P	20000824		
	US 2001-810671	A	20010319		
	WO 2001-US26389	W	20010824		
	US 2002-109854	A3	20020401		
	US 2003-339656	A3	20030110		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002016567	ICM	C12N009-00

US 2002076783 ECLA C12N009/12B1B
JP 2004522413 FTERM 2G045/AA25; 2G045/AA40; 2G045/BB03; 2G045/BB20; 2G045/CA25; 2G045/CB01; 2G045/CB03; 2G045/CB07; 2G045/CB08; 2G045/CB21; 2G045/DA12; 2G045/DA13; 2G045/DA14; 2G045/DA20; 2G045/DA36; 2G045/DA37; 2G045/DA77; 2G045/FB02; 2G045/FB03; 4B024/AA03; 4B024/AA11; 4B024/BA10; 4B024/CA04; 4B024/CA09; 4B024/EA04; 4B024/GA11; 4B024/HA12; 4B029/AA07; 4B029/AA23; 4B029/BB20; 4B029/CC03; 4B029/FA15; 4B050/CC01; 4B050/CC04; 4B050/DD11; 4B050/EE10; 4B050/LL01; 4B063/QA01; 4B063/QA18; 4B063/QQ03; 4B063/QQ08; 4B063/QQ13; 4B063/QQ20; 4B063/QQ27; 4B063/QQ41; 4B063/QR07; 4B063/QR32; 4B063/QR55; 4B063/QR77; 4B063/QR80; 4B063/QR82; 4B063/QS34; 4B065/AA26X; 4B065/AA46X; 4B065/AA50X; 4B065/AA72X; 4B065/AA88; 4B065/AA90X; 4B065/AA91X; 4B065/AB01; 4B065/AC14; 4B065/BA02; 4B065/CA29; 4B065/CA44; 4B065/CA53; 4C084/AA17; 4C084/NA14; 4C084/ZA891; 4C084/ZB111; 4C084/ZB212; 4C084/ZB261; 4C084/ZC021; 4C084/ZC022; 4H045/AA10; 4H045/AA11; 4H045/AA20; 4H045/CA40; 4H045/DA75; 4H045/DA89; 4H045/EA20; 4H045/FA72; 4H045/FA73; 4H045/FA74
US 2002119548 ECLA C12N009/12B1B
US 2003134319 ECLA C12N009/12B1B
US 2004152123 ECLA C12N009/12B1B

AB The invention provides protein and cDNA and genomic sequences for a novel human protein, which shares sequence homol. to a known protein kinase, and is related to the **serine-arginine**-rich protein kinase subfamily. The gene is expressed in the bone osteosarcoma cell line, breast, uterus leiomyosarcoma, fetal heart, infant brain, colon-juvenile granulosa tumor, colon-moderately differentiated adenocarcinoma, bone marrow hematopoietic stem cells, pooled human melanocyte, and pregnant uterus, normal nerve, leukopheresis, myeloid cell as well as leukocyte. Ten novel single nucleotide polymorphism sites (beyond the ORF or in intron regions) were identified. Thus, the present invention specifically provides isolated peptide and nucleic acid mols., methods of identifying orthologs and paralogs of the protein kinases, methods of identifying modulators of the protein kinases, and methods of diagnosis and treatment of diseases associated with the protein kinases.

ST protein kinase **serine arginine** rich sequence homolog human

IT Carcinoma
(adenocarcinoma, gene expression in; protein, gene and cDNA sequences of human protein kinase sequence homolog and diagnostic and therapeutic uses thereof)

IT Intestine, neoplasm
(colon, gene expression in; protein, gene and cDNA sequences of human protein kinase sequence homolog and diagnostic and therapeutic uses thereof)

IT Gene, animal
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(encoding protein kinase; protein, gene and cDNA sequences of human protein kinase sequence homolog and diagnostic and therapeutic uses thereof)

IT Brain
Heart
(fetal, gene expression in; protein, gene and cDNA sequences of human protein kinase sequence homolog and diagnostic and therapeutic uses thereof)

IT Microarray technology
Nucleic acid hybridization
(for detecting protein kinase gene in a biol. sample; protein, gene and

cDNA sequences of human protein kinase sequence homolog and diagnostic and therapeutic uses thereof)

IT Probes (nucleic acid)
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(for detecting protein kinase gene in a biol. sample; protein, gene and cDNA sequences of human protein kinase sequence homolog and diagnostic and therapeutic uses thereof)

IT Immunoassay
(for detecting protein kinase in a biol. sample; protein, gene and cDNA sequences of human protein kinase sequence homolog and diagnostic and therapeutic uses thereof)

IT Promoter (genetic element)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(for expressing protein kinase homolog; protein, gene and cDNA sequences of human protein kinase sequence homolog and diagnostic and therapeutic uses thereof)

IT Bone marrow
Hematopoietic precursor cell
Leukocyte
Mammary gland
Melanocyte
Nerve
Uterus
(gene expression in; protein, gene and cDNA sequences of human protein kinase sequence homolog and diagnostic and therapeutic uses thereof)

IT Myoma
Sarcoma
(leiomyosarcoma, gene expression in; protein, gene and cDNA sequences of human protein kinase sequence homolog and diagnostic and therapeutic uses thereof)

IT Diagnosis
(mol.; protein, gene and cDNA sequences of human protein kinase sequence homolog and diagnostic and therapeutic uses thereof)

IT Hematopoietic precursor cell
(myeloid, gene expression in; protein, gene and cDNA sequences of human protein kinase sequence homolog and diagnostic and therapeutic uses thereof)

IT Bone, neoplasm
Sarcoma
(osteosarcoma, gene expression in; protein, gene and cDNA sequences of human protein kinase sequence homolog and diagnostic and therapeutic uses thereof)

IT DNA sequences
Human
Molecular cloning
Protein sequences
Therapy
cDNA sequences
(protein, gene and cDNA sequences of human protein kinase sequence homolog and diagnostic and therapeutic uses thereof)

IT Genetic polymorphism
(single nucleotide, on protein kinase sequence homolog gene; protein, gene and cDNA sequences of human protein kinase sequence homolog and diagnostic and therapeutic uses thereof)

IT Antibodies and Immunoglobulins
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(to protein kinase; protein, gene and cDNA sequences of human protein kinase sequence homolog and diagnostic and therapeutic uses thereof)

IT Heart
(toxicity, fetal, gene expression in; protein, gene and cDNA sequences of human protein kinase sequence homolog and diagnostic and therapeutic uses thereof)

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IT   Bone marrow
     Nerve
        (toxicity, gene expression in; protein, gene and cDNA sequences of
        human protein kinase sequence homolog and diagnostic and therapeutic
        uses thereof)
IT   Animal
        (transgenic; protein, gene and cDNA sequences of human protein kinase
        sequence homolog and diagnostic and therapeutic uses thereof)
IT   401055-70-7P
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (amino acid sequence; protein, gene and cDNA sequences of human protein
        kinase sequence homolog and diagnostic and therapeutic uses thereof)
IT   401055-69-4   401055-71-8
     RL: BSU (Biological study, unclassified); PRP (Properties); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (nucleotide sequence; protein, gene and cDNA sequences of human protein
        kinase sequence homolog and diagnostic and therapeutic uses thereof)
IT   372092-80-3P, Protein kinase
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (sequence homolog; protein, gene and cDNA sequences of human protein
        kinase sequence homolog and diagnostic and therapeutic uses thereof)
IT   401056-82-4   401056-83-5
     RL: PRP (Properties)
        (unclaimed protein sequence; protein, gene and cDNA sequences of human
        protein kinase sequence homolog and diagnostic and therapeutic uses
        thereof)


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     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
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L1      1301511 S KINASE?
L2         1597 S SERINE (W) ARGININE
L3          326 S L1 AND L2
L4      7000132 S CLON? OR EXPRESS? OR RECOMBINANT
L5          207 S L3 AND L4
L6          116 S HUMAN AND L5
L7          696 S "SERINE ARGININE RICH"
L8           78 S L6 AND L7
                E BOYDS J Y/AU
                E YE J/AU
L9         1892 S E3
                E YAN C/AU
L10        1117 S E3
                E KETCHUM K A/AU
L11         480 S E3-E8
                E DIFRANCESCO V/AU
L12         117 S E3-E4
                E BEASLEY E M/AU
L13       31699 S E3\
L14         324 S E3
L15        3624 S L9 OR L10 OR L11 OR L12 OR L14
L16           1 S L2 AND L15

=> s l7 and l15
L17           1 L7 AND L15
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L17 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:157957 HCAPLUS
DOCUMENT NUMBER: 136:195349
TITLE: Protein, gene and cDNA sequences of human protein kinase sequence homolog and diagnostic and therapeutic uses thereof
INVENTOR(S): Yan, Chunhua; Ye, Jane; **Ketchum, Karen A.**; Di Francesco, Valentina; Beasley, Ellen M.
PATENT ASSIGNEE(S): Applera Corporation, USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002016567	A2	20020228	WO 2001-US26389	20010824
WO 2002016567	A3	20030130		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002076783	A1	20020620	US 2001-810671	20010319
US 6455291	B2	20020924		
CA 2421062	AA	20020228	CA 2001-2421062	20010824
AU 2001086687	A5	20020304	AU 2001-86687	20010824
EP 1313844	A2	20030528	EP 2001-966150	20010824
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JP 2004522413	T2	20040729	JP 2002-522241	20010824
US 2002119548	A1	20020829	US 2002-109854	20020401
US 6630337	B2	20031007		
US 2003134319	A1	20030717	US 2003-339656	20030110
US 6733978	B2	20040511		
US 2004152123	A1	20040805	US 2004-801671	20040317

PRIORITY APPLN. INFO.:		
US 2000-227470P	P	20000824
US 2001-810671	A	20010319
WO 2001-US26389	W	20010824
US 2002-109854	A3	20020401
US 2003-339656	A3	20030110

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(FILE 'HOME' ENTERED AT 11:22:18 ON 01 APR 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 11:22:41 ON 01 APR 2005

L1 1301511 S KINASE?
L2 1597 S SERINE (W) ARGININE
L3 326 S L1 AND L2
L4 7000132 S CLON? OR EXPRESS? OR RECOMBINANT
L5 207 S L3 AND L4

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L6          116 S HUMAN AND L5
L7          696 S "SERINE ARGININE RICH"
L8           78 S L6 AND L7
                E BOYDS J Y/AU
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L9         1892 S E3
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L11         480 S E3-E8
                E DIFRANCESCO V/AU
L12         117 S E3-E4
                E BEASLEY E M/AU
L13       31699 S E3\
L14         324 S E3
L15        3624 S L9 OR L10 OR L11 OR L12 OR L14
L16           1 S L2 AND L15
L17           1 S L7 AND L15

=> s l6 and l15
L18           1 L6 AND L15

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L18  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   2002:157957  HCAPLUS
DN   136:195349
ED   Entered STN:  01 Mar 2002
TI   Protein, gene and cDNA sequences of human protein kinase
     sequence homolog and diagnostic and therapeutic uses thereof
IN   Yan, Chunhua; Ye, Jane; Ketchum, Karen A.; Di Francesco,
     Valentina; Beasley, Ellen M.
PA   Applera Corporation, USA
SO   PCT Int. Appl., 81 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
IC   ICM  C12N009-00
CC   3-3 (Biochemical Genetics)
     Section cross-reference(s): 1, 7, 13
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
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PI   WO 2002016567        A2    20020228    WO 2001-US26389         20010824
     WO 2002016567        A3    20030130
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
             UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 2002076783        A1    20020620    US 2001-810671          20010319
     US 6455291           B2    20020924
     CA 2421062           AA    20020228    CA 2001-2421062         20010824
     AU 2001086687        A5    20020304    AU 2001-86687           20010824
     EP 1313844           A2    20030528    EP 2001-966150          20010824
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2004522413        T2    20040729    JP 2002-522241          20010824
     US 2002119548        A1    20020829    US 2002-109854          20020401
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	US 6630337	B2	20031007		
	US 2003134319	A1	20030717	US 2003-339656	20030110
	US 6733978	B2	20040511		
	US 2004152123	A1	20040805	US 2004-801671	20040317
PRAI	US 2000-227470P	P	20000824		
	US 2001-810671	A	20010319		
	WO 2001-US26389	W	20010824		
	US 2002-109854	A3	20020401		
	US 2003-339656	A3	20030110		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002016567	ICM	C12N009-00
US 2002076783	ECLA	C12N009/12B1B
JP 2004522413	FTERM	2G045/AA25; 2G045/AA40; 2G045/BB03; 2G045/BB20; 2G045/CA25; 2G045/CB01; 2G045/CB03; 2G045/CB07; 2G045/CB08; 2G045/CB21; 2G045/DA12; 2G045/DA13; 2G045/DA14; 2G045/DA20; 2G045/DA36; 2G045/DA37; 2G045/DA77; 2G045/FB02; 2G045/FB03; 4B024/AA03; 4B024/AA11; 4B024/BA10; 4B024/CA04; 4B024/CA09; 4B024/EA04; 4B024/GA11; 4B024/HA12; 4B029/AA07; 4B029/AA23; 4B029/BB20; 4B029/CC03; 4B029/FA15; 4B050/CC01; 4B050/CC04; 4B050/DD11; 4B050/EE10; 4B050/LL01; 4B063/QA01; 4B063/QA18; 4B063/QQ03; 4B063/QQ08; 4B063/QQ13; 4B063/QQ20; 4B063/QQ27; 4B063/QQ41; 4B063/QR07; 4B063/QR32; 4B063/QR55; 4B063/QR77; 4B063/QR80; 4B063/QR82; 4B063/QS34; 4B065/AA26X; 4B065/AA46X; 4B065/AA50X; 4B065/AA72X; 4B065/AA88; 4B065/AA90X; 4B065/AA91X; 4B065/AB01; 4B065/AC14; 4B065/BA02; 4B065/CA29; 4B065/CA44; 4B065/CA53; 4C084/AA17; 4C084/NA14; 4C084/ZA891; 4C084/ZB111; 4C084/ZB212; 4C084/ZB261; 4C084/ZC021; 4C084/ZC022; 4H045/AA10; 4H045/AA11; 4H045/AA20; 4H045/CA40; 4H045/DA75; 4H045/DA89; 4H045/EA20; 4H045/FA72; 4H045/FA73; 4H045/FA74
US 2002119548	ECLA	C12N009/12B1B
US 2003134319	ECLA	C12N009/12B1B
US 2004152123	ECLA	C12N009/12B1B

AB The invention provides protein and cDNA and genomic sequences for a novel **human** protein, which shares sequence homol. to a known protein **kinase**, and is related to the **serine-arginine** -rich protein **kinase** subfamily. The gene is **expressed** in the bone osteosarcoma cell line, breast, uterus leiomyosarcoma, fetal heart, infant brain, colon-juvenile granulosa tumor, colon-moderately differentiated adenocarcinoma, bone marrow hematopoietic stem cells, pooled **human** melanocyte, and pregnant uterus, normal nerve, leukopheresis, myeloid cell as well as leukocyte. Ten novel single nucleotide polymorphism sites (beyond the ORF or in intron regions) were identified. Thus, the present invention specifically provides isolated peptide and nucleic acid mols., methods of identifying orthologs and paralogs of the protein **kinases**, methods of identifying modulators of the protein **kinases**, and methods of diagnosis and treatment of diseases associated with the protein **kinases**.

ST protein **kinase serine arginine** rich sequence homolog **human**

IT Carcinoma
(adenocarcinoma, gene **expression** in; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT Intestine, neoplasm
(colon, gene **expression** in; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT Gene, animal
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(encoding protein **kinase**; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT Brain
Heart
(fetal, gene **expression** in; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT Microarray technology
Nucleic acid hybridization
(for detecting protein **kinase** gene in a biol. sample; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT Probes (nucleic acid)
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(for detecting protein **kinase** gene in a biol. sample; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT Immunoassay
(for detecting protein **kinase** in a biol. sample; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT Promoter (genetic element)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(for **expressing** protein **kinase** homolog; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT Bone marrow
Hematopoietic precursor cell
Leukocyte
Mammary gland
Melanocyte
Nerve
Uterus
(gene **expression** in; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT Myoma
Sarcoma
(leiomyosarcoma, gene **expression** in; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT Diagnosis
(mol.; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT Hematopoietic precursor cell
(myeloid, gene **expression** in; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT Bone, neoplasm
Sarcoma
(osteosarcoma, gene **expression** in; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT DNA sequences
Human

Molecular **cloning**
Protein sequences
Therapy
cDNA sequences
(protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT Genetic polymorphism
(single nucleotide, on protein **kinase** sequence homolog gene; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT Antibodies and Immunoglobulins
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(to protein **kinase**; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT Heart
(toxicity, fetal, gene **expression** in; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT Bone marrow
Nerve
(toxicity, gene **expression** in; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT Animal
(transgenic; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT 401055-70-7P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT 401055-69-4 401055-71-8
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT 372092-80-3P, Protein **kinase**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(sequence homolog; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

IT 401056-82-4 401056-83-5
RL: PRP (Properties)
(unclaimed protein sequence; protein, gene and cDNA sequences of **human** protein **kinase** sequence homolog and diagnostic and therapeutic uses thereof)

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(FILE 'HOME' ENTERED AT 11:22:18 ON 01 APR 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 11:22:41 ON 01 APR 2005

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L1      1301511 S KINASE?
L2         1597 S SERINE (W) ARGININE
L3          326 S L1 AND L2
L4      7000132 S CLON? OR EXPRESS? OR RECOMBINANT
L5          207 S L3 AND L4
L6          116 S HUMAN AND L5
L7          696 S "SERINE ARGININE RICH"
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                E BOYDS J Y/AU
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L11         480 S E3-E8
                E DIFRANCESCO V/AU
L12         117 S E3-E4
                E BEASLEY E M/AU
L13       31699 S E3\
L14         324 S E3
L15        3624 S L9 OR L10 OR L11 OR L12 OR L14
L16           1 S L2 AND L15
L17           1 S L7 AND L15
L18           1 S L6 AND L15
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1	L1	58173	kinase$2
2	L2	720395	clon$3 or express$3 or recombinant
3	L3	720	serine adj arginine
4	L4	34262	l1 same l2
5	L5	8	l3 adj3 l1
6	L6	36	l3 same l4
7	L7	474841	human
8	L8	18	l6 same l7
9	L9	21426	YAN YE KETCHUM DIFRANCESCO BEASLEY
10	L10	52	l3 and l9

	Issue Date	Pages	Document ID	Title
1	20040805	53	US 20040152123 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
2	20040722	55	US 20040142379 A1	Affinity fishing for ligands and proteins receptors
3	20030717	53	US 20030134319 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
4	20020829	53	US 20020119548 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
5	20020620	52	US 20020076783 A1	Plants and plants cells expressing histidine tagged intimin
6	20040511	50	US 6733978 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
7	20031007	50	US 6630337 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
8	20020924	50	US 6455291 B1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof

FILING FEE RECEIVED 1976	FEES: Authority has been given in Paper No. _____ to charge/credit DEPOSIT ACCOUNT No. _____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit

	Issue Date	Pages	Document ID	Title
1	20041223	20	US 20040259220 A1	CLK protein kinases and related products and methods
2	20041202	678	US 20040241653 A1	Methods for identifying marker genes for cancer
3	20041118	274	US 20040229367 A1	Methods for monitoring multiple gene expression
4	20040805	53	US 20040152123 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
5	20040701	130	US 20040127406 A1	Methods for in vitro expansion and transdifferentiation of human pancreatic acinar cells into insulin-producing cells
6	20040422	253	US 20040076955 A1	Methods of diagnosis of bladder cancer, compositions and methods of screening for modulators of bladder cancer
7	20040415	337	US 20040072160 A1	Molecular toxicology modeling
8	20040318	287	US 20040053245 A1	Novel nucleic acids and polypeptides
9	20040226	621	US 20040038292 A1	Wound healing biomarkers
10	20040212	570	US 20040029114 A1	Methods of diagnosis of breast cancer, compositions and methods of screening for modulators of breast cancer
11	20040122	146	US 20040014040 A1	Cardiotoxin molecular toxicology modeling
12	20040115	75	US 20040009489 A1	Classification of lung carcinomas using gene expression analysis

	Issue Date	Pages	Document ID	Title
13	20040115	484	US 20040009479 A1	Methods and compositions for diagnosing or monitoring auto immune and chronic inflammatory diseases
14	20031211	61	US 20030229204 A1	PCG-1, a novel brown fat PPARgamma coactivator
15	20031204	106	US 20030224411 A1	Genes that are up- or down-regulated during differentiation of human embryonic stem cells
16	20030731	42	US 20030143622 A1	Human RNA binding proteins
17	20030717	53	US 20030134319 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
18	20030605	54	US 20030104393 A1	Blood assessment of injury
19	20030417	83	US 20030073819 A1	PGC-1, a novel brown fat PPARgamma coactivator
20	20020829	53	US 20020119548 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
21	20020808	21	US 20020106771 A1	Nucleic acids encoding CLK protein kinases
22	20020801	33	US 20020104105 A1	Protein-protein interactions
23	20020627	61	US 20020082413 A1	PGC-1, a novel brown fat PPARgamma coactivator
24	20020620	52	US 20020076783 A1	Plants and plants cells expressing histidine tagged intimin

25	20050329	59	US 6872391 B2	PGC-1, a novel brown fat PPAR.gamma. coactivator

	Issue Date	Pages	Document ID	Title
26	20040928	32	US 6797513 B2	Nucleic acid encoding CLK2 protein kinases
27	20040511	50	US 6733978 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
28	20040316	434	US 6706867 B1	DNA array sequence selection
29	20031007	50	US 6630337 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
30	20030225	60	US 6525178 B2	PGC-1, a novel brown fat PPARgamma coactivator
31	20030225	39	US 6524579 B1	Human RNA binding process
32	20020924	50	US 6455291 B1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
33	20020730	59	US 6426411 B1	PGC-1, a novel brown fat ppar.gamma. coactivator
34	20001226	53	US 6166192 A	PGC-1, a novel brown fat PPAR.gamma. coactivator
35	20000201	39	US 6020164 A	Human RNA binding proteins
36	19960924	42	US 5559019 A	Protein serine kinase, SRPK1

	Issue Date	Pages	Document ID	Title
1	20041223	20	US 20040259220 A1	CLK protein kinases and related products and methods
2	20041118	274	US 20040229367 A1	Methods for monitoring multiple gene expression
3	20040805	53	US 20040152123 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
4	20040422	253	US 20040076955 A1	Methods of diagnosis of bladder cancer, compositions and methods of screening for modulators of bladder cancer
5	20040415	337	US 20040072160 A1	Molecular toxicology modeling
6	20040318	287	US 20040053245 A1	Novel nucleic acids and polypeptides
7	20040212	570	US 20040029114 A1	Methods of diagnosis of breast cancer, compositions and methods of screening for modulators of breast cancer
8	20040122	146	US 20040014040 A1	Cardiotoxin molecular toxicology modeling
9	20030717	53	US 20030134319 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
10	20030605	54	US 20030104393 A1	Blood assessment of injury
11	20020829	53	US 20020119548 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof

12	20020808	21	US 20020106771 A1	Nucleic acids encoding CLK protein kinases

	Issue Date	Pages	Document ID	Title
13	20020620	52	US 20020076783 A1	Plants and plants cells expressing histidine tagged intimin
14	20040928	32	US 6797513 B2	Nucleic acid encoding CLK2 protein kinases
15	20040511	50	US 6733978 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
16	20040316	434	US 6706867 B1	DNA array sequence selection
17	20031007	50	US 6630337 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
18	20020924	50	US 6455291 B1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof

	Issue Date	Pages	Document ID	Title
1	20050331	104	US 20050069878 A1	Proteins associated with cell growth, differentiation, and death
2	20041223	50	US 20040259802 A1	Anti-chrondrosarcoma compounds
3	20041216	67	US 20040254094 A1	Suppression of cyclin kinase activity for prevention and treatment of infections
4	20041021	67	US 20040210950 A1	Methods and compositions relating to muscle specific sarcomeric calcineurin-binding proteins (CALSARCINS)
5	20040923	67	US 20040186275 A1	Methods and compositions relating to muscle specific sarcomeric calcineurin-binding proteins (calsarcins)
6	20040812	102	US 20040157297 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
7	20040805	53	US 20040152123 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
8	20040701	67	US 20040127686 A1	Methods and compositions relating to muscle specific sarcomeric calcineurin-binding proteins (calsarcins)
9	20040701	60	US 20040127421 A1	Method to increase fibronectin
10	20040701	49	US 20040127420 A1	Metalloproteinase inhibitors for wound healing

11	20040527	154	US 20040101884 A1	Molecules for disease detection and treatment

	Issue Date	Pages	Document ID	Title
37	20020704	24	US 20020086427 A1	Inducible eukaryotic expression system that regulates protein translation
38	20020620	52	US 20020076783 A1	Plants and plants cells expressing histidine tagged intimin
39	20020418	105	US 20020045253 A1	METHODS COMPRISING APOPTOSIS INHIBITORS FOR THE GENERATION OF TRANSGENIC PIGS
40	20040622	98	US 6753175 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
41	20040511	50	US 6733978 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
42	20040106	10	US 6673108 B2	Transmural concentric multilayer ingrowth matrix within well-defined porosity
43	20031021	179	US 6635623 B1	Lipoproteins as nucleic acid vectors
44	20031007	50	US 6630337 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
45	20030211	39	US 6518400 B1	Polynucleotide encoding a protein involved in chromosomal inheritance and method of use therefor
46	20030107	104	US 6503703 B1	Identification and use of antiviral compounds that inhibit interaction of host cell proteins and viral proteins required for viral replication

	Issue Date	Pages	Document ID	Title
47	20021210	95	US 6492153 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
48	20021001	52	US 6458559 B1	Multivalent RNA aptamers and their expression in multicellular organisms
49	20020924	50	US 6455291 B1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
50	20020409	100	US 6369294 B1	Methods comprising apoptosis inhibitors for the generation of transgenic pigs
51	20011030	26	US 6309830 B1	Human suppressor tRNA oligonucleotides and methods of use for same
52	20010807	99	US 6271436 B1	Cells and methods for the generation of transgenic pigs